U.S. DEPARTMENT OF COMMERCE
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PB-255 582

WASTE TREATMENT AND DISPOSAL METHODS FOR THE PHARMACEUTICAL INDUSTRY

NATIONAL FIELD INVESTIGATIONS CENTER

MARCH 1975

S- 1

212033

PB 255 582

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U. S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA. 22161

BIBLIOGRAPHIC DATA SHEET

1. Report No.
EPA/330/1-75/001

2.

3. Recipient's Accession No.
PB-255 582

4. Title and Subtitle
Waste Treatment and Disposal Methods for the Pharmaceutical Industry,

5. Report Date
Mar 75

6.

7. Author(s)
E. J. Struzeski, Jr.

8. Performing Organization Rept. No.

9. Performing Organization Name and Address
National Field Investigations Center-Denver, Colo.

10. Project/Task/Work Unit No.

11. Contract/Grant No.

12. Sponsoring Organization Name and Address

13. Type of Report & Period Covered

14.

15. Supplementary Notes

16. Abstracts

Contents: Industry categorization--Standard Industrial Classification, Kline Guide, Gulf South Research Institute, National Field Investigations Center-Denver; Process description--Unit processes, Typical plant operations); Waste characteristics--(Fermentation, Synthesized organic chemicals), Biologicals, Drug formulation, Waste parameters of significance, BOD: A Question of reliability, Toxicity, Nitrogen reduction), Waste recovery and control-- Solvent recovery, By product recovery-antibiotics production, Byproduct recovery-technological transfer, Wastewater reduction and recovery methods), Waste treatment and disposal-- Activated sludge, Trickling filtration, Other treatment methods); Development of effluent limitations--Exemplary plant, Available Treatment and Disposal processes, Model systems, Effluent limitations, Bibliography, Case histories of the pharmaceutical industry).

17. Key Words and Document Analysis. 17a. Descriptors

*Drug industry
*Industrial waste treatment,
*Water pollution control

Organic compounds,
Process charting,
Manufacturing,
Design criteria,
Effluents,
Fermentation,
Sludge,
Formulation,
Filters,
Anaerobic conditions,
Materials recovery,
Distillation,
Toxicity,
Nitrogen organic compounds,
Byproducts,
Waste disposal,
Heavy metals,
Solid waste disposal,
Sewage treatment.

17b. Identifiers/Open-Ended Terms

Biological industrial waste treatment,
Liquid waste disposal.

17c. COSATI Field/Group 7 A,

18. Availability Statement
National Technical Information Service
Springfield, Va. 22161

19. Security Class (This Report)
UNCLASSIFIED

20. Security Class (This Page)
UNCLASSIFIED

21. No. of Pages
295

22. Price
$9.25/$2.25

FORM NTIS-35 (REV. 10-73) ENDORSED BY ANSI AND UNESCO. THIS FORM MAY BE REPRODUCED USCOMM-DC 8265-P74

ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF ENFORCEMENT

WASTE TREATMENT AND DISPOSAL METHODS
FOR THE
PHARMACEUTICAL INDUSTRY

by

E. J. Struzeski, Jr.

National Field Investigations Center
Denver, Colorado

March 1975

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CONVERSIONS

multiply *Metric Unit**	*by*	*to obtain* *English Unit*
°Celcius (°C)	9/5 (°C) + 32 (absolute: 9/5 °C)	°Fahrenheit (°F)
centimeters (cm)	0.394	inches (in)
cubic meters (m^3)	35.32	cubic feet (ft^3)
	1.307	cubic yards (yd^3)
	0.035	bushels (bu)
	264.2	gallons (gal)
grams (g)	0.035	ounces (oz)
hectares (ha)	2.471	acres
kilograms (kg)	2.205	pounds (lb)
liters (l)	0.264	gallons (gal)
	1.057	quarts (qt)
meters (m)	3.281	feet (ft)
	1.094	yards (yd)
metric tons	1.102	short tons (tons)
micrometer (μm)	0.039	inches (in)
million gallons/day (mgd)	3,770	cubic meters/day (m^3/day)
square meters (m^2)	10.76	square feet (ft^2)
	1.196	square yards (yd^2)
	2.471×10^{-4}	acres

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*Metric prefixes:
mega (M)......10^6
kilo (k)......10^3
hecto (h).....10^2
deca (da).....10^1
deci (d)......10^1
centi (c).....10^{-2}
milli (m).....10^{-3}
micro (μ).....10^{-6}

ABBREVIATIONS

ASTM	American Society for Testing and Materials
avg	average
BOD	biochemical oxygen demand (BOD$_5$ unless otherwise indicated)
COD	chemical oxygen demand
cpm	cycles per minute
DO	dissolved oxygen
FDA	Federal Drug Administration
F/M	Food to micro-organism ratio
FWQA	Federal Water Quality Administration
gpd	gallons per day
gpm	gallons per minute
gsfpd	gallons per square foot per day
hp	horsepower
hr	hour
IU	International Units
kwh	kilowatthour
μ	micron
μm; μg	micrometer; microgram
mgd	million gallons per day
ML(V)SS	mixed liquor (volatile) suspended solids
MSG	monosodium glutamate
NOD	nitrogenous oxygen demand
OH^-	(hydroxide group)
O&M	operations & maintenance
PE	population equivalents
pH	(hydrogen-ion activity)
ppb	parts per billion
ppm	parts per million
psi(a)	pounds per square inch (absolute)
psig	pounds per square inch gage
Pt-Co units	Platinum-Cobal units
SRT	solids retention time
TDS	total dissolved solids
TL_m	median toxic limit
TOC	total organic carbon
TS	total solids
TSS	total suspended solids
TVS	total volatile solids

I. INTRODUCTION

In early 1974, NFIC-D was asked by EPA Regions II, III, IV and V to prepare National Pollutant Discharge Elimination System (NPDES) permits for ten major pharmaceutical manufacturing plants in Pennsylvania, Virginia, Indiana and Puerto Rico. Effluent guidelines, the basis for establishing effluent limitations specified in the permits, had not been developed for the pharmaceutical industry. It was thus necessary to develop a rationale for establishing effluent limitations that would fulfill two requirements. They must be neither too lenient nor too stringent relative to prevailing waste treatment and control practices in the industry, and waste treatment improvements necessary to meet assigned limitations must be practicable.

The ten specified plants were visited to obtain process descriptions, information on waste treatment facilities and wasteload data. Also, available literature on these plants was reviewed. Because of the diversity of manufacturing and waste treatment processes at the ten plants, as well as the different levels of treatment efficiency achieved, a review of waste treatment and control practices at other pharmaceutical plants became necessary to develop an acceptable rationale. The study was expanded to include visits to five additional plants and an extensive literature review of 120 articles covering all aspects of waste treatment and control in the industry. In all, data were collected on 39 pharmaceutical plants.

Case histories (see Appendix) were prepared for nine of the ten plants for which permits were drafted (listed on the following page). These case histories summarize available literature on production processes, waste treatment and control and wasteloads at each plant, give detailed information on current waste treatment facilities, summarize recent wasteload data, and present effluent limitations established for each plant.

Commercial Solvents Corporation, Terre Haute, Ind. (3)[†]
Eli Lilly and Co., Clinton Laboratories, Clinton, Ind. (3)
Eli Lilly and Co., Mayaguez, Puerto Rico (2)
Eli Lilly and Co., Tippecanoe Laboratories, Lafayette, Ind.(3)
McNeil Laboratories, Fort Washington, Pa. (5)
Merck and Company, Inc., Cherokee Plant, Danville, Pa. (3)
Merck and Company, Inc., Stonewall Plant, Elkton, Va. (3)
Pfizer, Inc., Terre Haute, Ind. (3)
Wyeth Laboratories, Marietta, Pa. (4,5)
Wyeth Laboratories, Paoli, Pa. (5)

To expand the data base for developing the effluent limitations, varying combinations of literature review and plant visits were used for these additional 29 plants:

Abbott Laboratories, North Chicago, Ill. (3,5)*
Abbott Laboratories, Sidney, Australia (3)
Abbott Laboratories, Barceloneta, Puerto Rico (3)
American Cyanamid Co., Calco Chemical Division,
    Willow Island, W. Va. (3)
Berkeley Chemicals Division, Summit, N.J. (2)
Boots Pure Drug Co., Ltd., Nottingham, Great Britain (2)
Bristol Laboratories, Syracuse, N.Y. (3)
Dorsey Laboratories, Lincoln, Neb. (5)
Eli Lilly Greenfield Laboratories, Greenfield, Ind. (4)
Hoffman-LaRoche, Belvidere, N.J.(2)*
Hoffman-LaRoche, Nutley, N.J.(3)
Lederle Laboratories, Pearl River, N.Y. (3,4)*
Merck and Company, Inc., Albany, Ga. (2)
Merck and Company, Inc., West Point, Pa. (5)
Merck and Company, Inc., Barceloneta, Puerto Rico (2)
M/s Indian Drugs and Pharmaceuticals, Hyderabad, India (2)
Parke-Davis and Co., Holland, Mich. (2,3)
Parke-Davis and Co., Hounslow, Great Britain (2)
Pfizer, Inc., Groton, Conn. (3)
Pfizer, Inc., Brooklyn, N.Y. (3)
Pfizer, Inc., Folkestone, Great Britain (5)
Pfizer, Inc., Sandwich, Kent, Great Britain (3)
Salisbury Laboratories, Charles City, Iowa (2)
Schering-Plough, Inc., Kenilworth, N.J. (5)
Schering-Plough, Inc., Union, N.J. (3)*
Squibb, E.R. and Sons, Inc., Humacao, Puerto Rico (2)
Upjohn Company, Kalamazoo, Mich. (3)
Warner-Chilcott, Morris Plains, N.J. (5)*
Wyeth Laboratories, West Chester, Pa. (3)

This study thus evolved into a broad and detailed review of waste treatment and control practices in the pharmaceutical industry.

[†] Parenthetic numbers indicate NFIC-D industrial categories, described in Section III

* Plants visited

Although difficult to define, the pharmaceutical industry is generally involved in the production of medicinal chemicals, biologicals, and botanicals having therapeutic value for humans and animals. Products of the industry are used for industrial, agricultural, and domestic purposes and are found in such familiar forms as cleaning agents, pesticides, fertilizers, cosmetics and baked goods.* The industry is growing at the rate of 9 percent annually. In 1973, an estimated $1.4 billion of medicinals ($665 million), biologicals ($540 million) and botanicals ($185 million) were sold as pharmaceuticals or food and feed supplements.

The pharmaceutical industry employs a vast array of complex processes, many of which are proprietary. This report is not intended to be an exhaustive presentation of such processes; appropriate texts of pharmaceuticals and chemical engineering will provide greater detail on processes. However, pertinent processes are discussed in sufficient detail to establish the unit processes involved at plants of interest as they determine wasteloads and characteristics.

Wastes from pharmaceutical operations are extremely strong and concentrated, difficult to handle, and require some of the most complex and expensive treatment and control systems of any industry. This report presents a detailed description of waste characteristics and current waste treatment and control practices in the industry.

The information derived from this study of the pharmaceutical industry is presented in ten main sections of this report, including: Summary, Industrial Categorization, Process Description, Waste Characterization, Waste Parameters of Significance, Waste Recovery and Control, Waste Treatment and Disposal, Development of Effluent Limitations, and Case Histories (Appendix).

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* For an extensive list of pharmaceutical products see: *Pharmaceuticals* (104), *Drugs in Current Use and New Drugs* (85), *Chemistry in the Economy* (116), *The Merck Index* (71).

II. SUMMARY

This report provides the rationale for establishing effluent limitations which were used by NFIC-D in preparation of NPDES permits for ten major pharmaceutical manufacturing industries in the United States and Puerto Rico. Establishing the effluent limitations entailed plant visits, data collection and evaluation, and an extensive literature review for 39 plants. Thus, this report serves as a state-of-the-art review of current waste treatment and control technology existing throughout the pharmaceutical industry.

Information derived from the study is condensed in the following Section summaries.

INDUSTRY CATEGORIZATION

A wide variety of processes and raw materials are used by the pharmaceutical industry to produce a broad spectrum of final products. The characteristics of resulting wastewaters are equally varied. To facilitate evaluation of waste treatment practices, the industry was divided into categories having similar processes, waste disposal problems and waste treatment practices.

Five major categories were defined. *Fermentation Plants* employ fermentation processes to produce medicinal chemicals. In contrast, *Synthesized Organic Chemicals Plants* produce medicinal chemicals (fine chemicals) by organic synthesis processes. Most plants are actually combinations of these two, yielding the third category, *Fermentation/Synthesized Organic Chemicals Plants*. *Biologicals Production Plants* produce vaccines and antitoxins. In the final category, the *Drug Mixing, Formulation and Preparation Plants* produce pharmaceutical preparations in final form, such as tablets and capsules.

PROCESS DESCRIPTION

Process Description includes many typical manufacturing schemes, unit processes, and typical plant operations. Unit processes are enumerated for fermentation, synthesized organic chemicals, biologicals production and for drug formulation. Under fermentation are described fermentation media, the chemistry and some of the manufacturing steps for vitamins, particularly vitamins B_2, B_{12}, and C; citric acid; the antibiotics, particularly penicillin, Terramycin, and streptomycin; and also enzymes production. Penicillin preparation is explained for Bristol Laboratories and Wyeth Laboratories. The Terramycin process is detailed both in theory and actual production at two Pfizer, Inc. plants in Great Britain.

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Synthesis of organic chemicals focuses on chemistry and typical or special operations necessary for vitamins B_2 and C, the synthetic antibiotic Chloromycetin, the broad group of sulfa drugs, and the important classifications of steroids and prostglandins. Chloromycetin processing is illustrated for the Parke-Davis plants at Hounslow, Great Britain and Holland, Mich. Special attention is devoted to the early Upjohn Co. process for cortisone, the first important steroid. Cortisone was a forerunner in steroid chemistry and many ensuing discoveries. Steroids include the anti-inflammatory agents, sex hormones, tissue building agents and contraceptives. Prostglandins represent one of newest of pharmaceutical chemicals available. They simulate functions of the prostrate gland in the body but their reactions are still yet largely unknown. Filtration techniques as employed in pharmaceutical works are related to intended uses, and absolute and depth-type filters are compared.

Description is also given of typical drug formulation, mixing and packaging operations leading to final products as purchased in the local drug store.

WASTE CHARACTERISTICS

This Section of the report reviews major types of waste resulting from fermentation, synthesized organic chemicals and biologicals production. Specific waste sources and general character of wastes are cited. Data are presented for penicillin, streptomycin and steroids manufacturing with emphasis on the composition of fermentation broths and their handling and disposal. BOD content of spent fermentation beers can exceed 35,000 mg/l. The disposition and degree of solvent and mycelium recovery will greatly influence waste strength and loads. Characterization of waste streams from synthesized organic chemicals production is given for Squibb, Inc., Humacao, Puerto Rico (synthetic penicillin and antifungals), Berkeley Chemicals Division, Summit, N. J. (various chemicals), Parke-Davis and Co., Holland, Mich. (largely Chloromycetin), and M/s Indian Drugs, Hyderabad, India. Extensive technical data on products, type of waste, and toxicity rating culminating from more than ten years of study at M/s Indian Drugs are given.

Synthesized chemical production wastes are strong, difficult to treat, and frequently inhibitory to biological treatment systems. Chemical wastes from the factory can change significantly from day to day. Biological production wastes are strong and contain animal remains, culture media, pathogenic organisms, toxic elements, and possibly pesticidal traces. Information is made available on waste characteristics associated with the antitoxins, antisera and vaccines production facility of Eli Lilly at Greenfield, Indiana.

WASTE PARAMETERS OF SIGNIFICANCE

Special attention is given to studies dealing with BOD, toxicity, and nitrogen reduction. Major parameters of importance in the pharmaceutical industry include BOD_5 and long-term BOD, COD, TOC, solids, pH, a wide array of trace metals and other troublesome ions potentially present, unoxidized nitrogen, phosphorous, color, odor, temperature and toxicity of pharmaceutical effluents.

Difficulties have been cited in using "Standard Methods" or equivalent procedures in analyzing some pharmaceutical wastes. Concern has been expressed on validity of the BOD test due to toxicity. Nitrification has also been reported during the course of the 5-day BOD test, causing further difficulty. Opinion seems fairly evenly divided on appropriateness of BOD. COD or TOC would serve to augment BOD results in the event of question. Toxicity impact upon biological treatment systems was described using various antibiotics, a phenol-mercury compound having bactericidal properties, the female sex hormone DES, and formaldehyde and methyl alcohol wastes. The alcohol and formaldehyde wastes showed no toxicity. DES could be degraded by activated sludge but only over unusually long treatment periods. The antibiotics demonstrated toxicity, but the biological system could be acclimated. In some cases, activated sludge could successfully treat the phenol-mercury waste, whereas in other cases the biological system could tolerate but not adequately degrade this waste.

Ammonia and organic nitrogen levels in typically treated pharmaceutical waste may range upward to a few hundred or as much as a few thousand mg/l when expressed as Kjeldahl nitrogen. Nitrogen loads may be appreciably high as to even exceed BOD effluent loads. Discharge loads have been reported in the range of 454 kg (1,000 lb)/day to 3,360 kg (8,000 lb)/day. Methods used in removing and reducing the various forms of unoxidized and oxidized nitrogen are reviewed.

WASTE RECOVERY AND CONTROL

Industry situations are described which have significantly reduced waste problems by recovery of valuable solvents, recovery of selected waste streams, especially spent fermentation broth as animal feeds, and specific wastewater reduction and recovery programs instituted by certain companies. The collection, evaporation and sale of dried fermentation solids has not only been practiced in the pharmaceutical field but has been implemented by the distilling and brewing industries as far back as the early 1950's. A number of cases are documented on fermentation solids recovery.

A Hiram Walker distillery without feed recovery had a wasteload of 50 to 55 population equivalents of BOD per bushel of grains processed. With an "entire plant" approach to recovery and without resorting to customary conventional treatment, the distillery showed 5.6 PE/bu grains in 1951-52. By virtue of further improvements, the Company reduced its wasteload to about 1.25 PE/bu grains, equivalent to about a 96 to 97 percent waste reduction.

In pharmaceutical manufacturing, the value of nutrients and undetermined growth factors contained in fermentation broth solids is thought quite high when used as animal feeds. Examples of fermentation solids recovery include Abbott Laboratories at North Chicago, Ill., the Upjohn Company, Kalamazoo, Mich., and Abbott Laboratories, Barceloneta, Puerto Rico. Detailed information is presented on these practices, including cost data for Abbott and Upjohn. Both Pfizer, Inc., Terre Haute, Ind. and Lederle Laboratories at Pearl River, N. Y. previously evaporated spent fermentation beers throughout the 1950's and 1960's, but they have subsequently discontinued such practice. Abbott, North Chicago in 1972-73 recovered beers with a BOD_5 load potential of 20,000 lb/day or greater, and together with activated sludge these practices were responsible for the overall plant BOD removals achieved of 98.7 percent. Upjohn reported that BOD reductions directly due to triple-effect evaporation ranged from 96 to 98 percent for four different types of antibiotic spent beers. Recovery of spent beers saves on expensive alternative biological treatment.

Intense recovery of solvents represents an extremely important aspect for pharmaceutical plants. A commercial ketone solvent was reported as having a BOD of approximately 2 million mg/l, or some 9,000 times stronger than untreated domestic sewage. A gallon of this solvent was calculated as equivalent in BOD to the sewage coming from a city of 77,000 people. Amyl acetate, another common solvent, is reported to have a BOD strength of about 1 million mg/l, and acetone shows a BOD of about 400,000 mg/l. A very small variation in quantity of solvents lost to the plant sewer can have a strong impact on treatment facilities and the receiving stream.

A preventive program at the Upjohn Company, Kalamazoo, Mich. in the mid-1950's served to reduce raw chemical wastes from a peak flow of 2,840 m^3 (750,000 gal)/day to 284 m^3 (75,000 gal)/day. BOD loads correspondingly dropped from 13,600 kg (30,000 lb)/day to about 1,360 kg (3,000 lb)/day. These reductions were in part due to installation of a spent solvents incineration system.

Bristol Laboratories, Syracuse, N.Y., in the 1950's prior to waste control implementation, showed a BOD of 0.74 PE/gal fermentation wastes. When contaminated or spoiled fermentation batches were controlled and with improved monitoring and recovery of solvents, Bristol Laboratories lowered their wasteload to about 0.29 PE/gal, or a 61 percent BOD reduction.

WASTE TREATMENT AND DISPOSAL

The pharmaceutical industry employs a wide variety of waste treatment and disposal methods, and therefore this Section of the report contains extensive information on the unique and different approaches taken by various companies. This Section has been divided into Activated Sludge, Trickling Filtration, and Other Treatment Methods. The latter includes data on anaerobic filters, spray irrigation, oxidation ponds, sludge stabilization, and deep well injection.

The literature gives some perspective on the merits of handling strong and sometimes toxic pharmaceutical wastes by activated sludge vs trickling filters. Trickling filter installations appear somewhat more prevalent in Great Britain compared to a greater predominance of activated sludge in the U. S. Two of the better performing activated sludge installations are at Abbott Laboratories, North Chicago, Ill. and Hoffman-LaRoche, Belvidere, N. J. Extensive technical information was compiled for these two diversified pharmaceutical manufacturing plants. The available data represents the equivalent of case history documentation for both Abbott and Hoffman-LaRoche.

Some wastes may be resistant to biodegradation by activated sludge, such as certain nitroaniline forms used in the production of sulfanilamides and the phenol-mercury waste (cited earlier in the report). Examples of activated sludge waste treatment are illustrated for E. R. Squibb, Humacao, Puerto Rico, M/s Indian Drugs and Pharmaceuticals, Hyderabad, India, Wyeth Laboratories at West Chester, Pa., Lederle Labs, Pearl River, N.Y., and Dorsey Labs at Lincoln, Nebr.

Wyeth Labs and Lederle Labs, the latter recently incorporating the Unox pure oxygen aeration process, represent examples of extensive pretreatment followed by secondary treatment by the municipal works. Overall BOD reductions for the Wyeth and Lederle wastes are about 97 to 98 percent.

Hoffman-LaRoche has a unique sodium sulfate recovery complex which receives select waste streams primarily from sulfa drug manufacturing. The recovery process consists of a fluidized bed followed by evaporation and drying of the salt. The most interesting features at Abbott's multi-million dollar treatment facility at North Chicago, Ill. are thought to be pasteurization of plant effluent in place of chlorination and a spent fermentation beer recovery system integral with an extensive incinerator ducting system. Exhaust air, from the drying of the spent beers, is taken into a specially-designed duct system and carried to the main plant boilers and incinerated. Other odorous air streams collected into the duct system include exhaust from the fermenters, and vents from the enclosed activated sludge tanks, degassing chambers and sludge holding tanks.

The activated sludge process, with adequate waste equalization and proper sludge disposal, has been shown to operate well at drug formulation and other pharmaceutical plants. Treatment of pharmaceutical wastes may become very difficult due to extreme variation in manufacturing levels, product mix and consequently in waste volume and strength. Because of batch processing, a 5-day work week and an 8 to 10 hr work day at many plants, considerable waste holding and treatment system recycling may be required especially over weekends. Waste equalization of about 2 to 3 days may be essential at certain establishments. Poor removal efficiencies may not be the fault of the treatment system but often can be attributed to lack of control by management over waste quantities. Since manufacturing expansion can occur frequently, and also due to other factors, treatment plant design criteria are too often exceeded. High diligence and control must be continuously maintained, owing to the special nature of pharmaceutical wastes.

Trickling filter installations and their performance in treating pharmaceutical waste are described for the Upjohn Company, Kalamazoo, Mich., American Cyanamid at Willow Island, W. Va., Lederle Laboratories at Pearl River, N. Y., Eli Lilly and Co. at Greenfield, Ind., and the Merck, Sharpe and Dohme plant at West Point, Pa. Furthermore, the Appendix contains trickling filter data for the Merck and Co., Inc., Elkton, Va. pharmaceutical plant.

The Upjohn Company, Kalamazoo, Mich. in the 1950's successfully handled spent fermentation beers by two-stage trickling filtration. Pharmaceutical wastes amounting to 2,270 m^3/day (600,000 gpd) and containing about 1,400 kg (3,100 lb) BOD/day demonstrated BOD reductions in the range of 95 to 98 percent. Influent and effluent BOD concentrations averaged 600 mg/l and 20 mg/l, respectively.

Wastes from the Merck, Sharpe and Dohme manufacturing plant, West Point, Pa., in the 1950's were subjected to two-stage high-rate trickling filtration providing high treatment performance. The raw wastes approximated 378 m^3 (100,000 gpd) with an average of 330 kg (725 lb) BOD/day. Overall BOD and TSS reductions were reported by the Company as greater than 98 and 91 percent, respectively. Experiences in Great Britain have shown that single- and multiple-stage filters can accept heavy loadings of mixed fermentation and other spent effluents and provide about 96 percent waste reduction. Trickling filters were also noted as being less susceptible to shock loads compared to other forms of treatment.

Anaerobic filters represent a potentially promising method of treating pharmaceutical wastes. Large-scale spray irrigation of pharmaceutical wastes has been employed in at least two known instances. The Upjohn Co., Kalamazoo, Mich. in the 1950's used spray irrigation as the principal means of disposing of heavy organic wastes, largely antibiotic spent broths. Including a series of waste connections to the city, the Commercial Solvents Corporation plant at Terre Haute, Ind. achieves an overall 91 percent BOD reduction. This is noteworthy since the remaining 9 percent wastes receive no treatment.

Other available treatment across the industry includes deep well disposal used by Parke-Davis, Holland, Mich., Abbott Laboratories at Barceloneta, Puerto Rico and the Upjohn Company, Kalamazoo, Mich. Incineration of concentrated organic wastes is found at a number of plants including Abbott Laboratories, Barceloneta, Puerto Rico; Abbott Laboratories, North Chicago, Ill.; Upjohn Co., Kalamazoo; Eli Lilly, Clinton, Ind.; Eli Lilly, Lafayette, Ind.; Eli Lilly, Mayaguez, Puerto Rico; E. R. Squibb, Humacao, Puerto Rico; Lederle Laboratories, Pearl River, N. Y.; and Merck and Co., Inc., Danville, Pa.

DEVELOPMENT OF EFFLUENT LIMITATIONS

Once the prescribed information was gathered and properly analyzed by NFIC-Denver, distinct categories of pharmaceutical plants were established, and plants achieving high performance levels of treatment were identified. From these plants together with other data, model systems were selected for each industrial category to define wasteload reduction currently attainable by well designed and operated waste treatment and control systems. Effluent limitations were then developed for important waste parameters in each category, based on performance levels of the model systems.

The more sophisticated waste treatment and control facilities at pharmaceutical plants almost always consisted of activated sludge and/or trickling filtration processes deployed as multistage systems. These systems appeared nearly equally applicable to all types of pharmaceutical establishments. With the exception of Abbott Laboratories at Barceloneta, Puerto Rico, Eli Lilly's Clinton Laboratories, and Commercial Solvents Corporation, Terre Haute, Ind., the known plants all employ some variation of the activated sludge process.

This Section, in addition to the model systems, describes alternative treatment and disposal techniques available today throughout the industry. Effluent limitations were developed in terms of percentage reductions in raw wasteloads or final effluent concentrations for parameters of significance. Recommended average daily limits for categories 1, 2 and 3 were set at 95.0 percent BOD removal, 82.0 percent COD removal, 82.5 percent TSS reduction and 75.0 percent ammonia nitrogen reduction. For categories 4 and 5, BOD and COD reductions were established as a minimum of 92.5 and 80.0 percent, respectively. Limits for metals and trace ions in pharmaceutical effluents have been suggested. Also, pH and fecal coliform limits and toxicity criteria are given for necessary inclusion in NPDES permits.

APPENDIX: CASE HISTORIES

The Appendix contains case histories prepared for nine pharmaceutical plants. As a result of many meetings, a considerable data base incorporating much technical information was compiled for each of the companies. The data spectrum was analyzed, NPDES permits were completed, and conclusions were drawn therefrom for the overall pharmaceuticals report. Plants described in the Appendix include:

Case History	Plant and Location	Category	Available Treatment
A	Eli Lilly and Co. Clinton Laboratories Clinton, Ind.	3	Chemical destruction, principally Carver-Greenfield evaporators and John Zink units
B	Eli Lilly and Co. Tippecanoe Laboratories Lafayette, Ind.	3	Multistage activated sludge, John Zink unit

Case History	Plant and Location	Category	Available Treatment
C	Pfizer, Inc. Vigo Plant Terre Haute, Ind.	3	Multistage activated sludge, aerobic stabilization plus standard and high-rate trickling filtration
D	Commercial Solvents Corporation Terre Haute, Ind.	3	Spray irrigation, connection to the city
E	Merck and Co., Inc. Stonewall Plant Elkton, Va.	3	Multistage activated sludge and trickling filtration
F	Merck and Co., Inc. Cherokee Plant Danville, Pa.	3	Activated sludge plus roughing trickling filter
G	Wyeth Laboratories Marietta, Pa.	4,5	Activated sludge
H	Wyeth Laboratories Paoli, Pa.	5	Activated sludge
I	McNeil Laboratories Fort Washington, Pa.	5	Activated sludge

III. INDUSTRY CATEGORIZATION

The pharmaceutical industry uses a wide variety of processes to produce an even broader variety of final products. The characteristics of wastewaters resulting from the various processes differ substantially, necessitating different approaches to waste treatment. Limitations on the wasteloads discharged by a pharmaceutical manufacturing facility must take into account these variations in waste characteristics and treatment. To achieve a uniform and equitable application of effluent limitations to substantially different pharmaceutical plants, it is desirable to divide the industry into categories of plants with similar operational characteristics. Several approaches to categorizing the industry were found in the literature review.

SIC

A common means of grouping industrial plants is the Standard Industrial Classification (SIC)(28)*. For the "drug industry," three broad SIC groups have been established as follows:

Biological Products (SIC-2831) -- Establishments primarily engaged in the production of bacterial and virus vaccine, toxoids serums, plasmas, and blood derivatives for human or veterinary use.

Medicinal Chemicals and Botanical Products (SIC-2833) -- Establishments primarily engaged in manufacturing bulk inorganic and organic medicinal chemicals and their derivatives and processing of bulk botanical drugs and herbs.

Pharmaceutical Preparations (SIC-2834) -- Establishments primarily engaged in fabricating or processing drugs into pharmaceutical preparations, mostly in finished form for human and veterinary use. Products include ampules, tablets, capsules, vials, ointments, medicinal powders, solutions and suspensions.

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* Bibliography entries are referred to throughout the text parenthetically; see p 153 for listing.

These SIC groupings are primarily based on final products. There are substantial differences in processes and waste characteristics among these three groups, as discussed in later sections of this report. From the process and waste characteristic viewpoint, however, there are also major variations within the Medicinal Chemicals and Botanicals group. A categorization different from the SIC groups is thus needed.

KLINE GUIDE

The Kline Guide to the Chemical Industry-1974 (46) includes as "bulk pharmaceuticals" the medicinal chemicals, biologicals, and botanicals having therapeutic value for humans or animals in the forms of pills, capsules, syrups, injectables, and ointments. Bulk pharmaceuticals are manufactured by a wide variety of processes, including chemical synthesis, fermentation, extraction, and other complex methods. The list on the following page presents pharmaceuticals according to the Guide.

The Kline Guide groups are based entirely on products and do not differentiate by process or waste characteristics. Thus the Guide does not present a suitable categorization scheme.

GSRI

A report on the State-of-the-Art on Pollution Control in the Pharmaceutical Industry (3) was prepared in 1973-74 by Gulf South Research Institute (GSRI) for the EPA and the Pharmaceutical Manufacturers Association (PMA). Based on that report and findings of GSRI, pharmaceutical plants were thus categorized:

Pharmaceutical

Chemical and Pharmaceutical/Chemical

All Others - combining two or more of the following groups: pharmaceutical compounding and formulating, chemical, fermentation, biological, and natural product extraction operations

These categories are not suitably definitive for the application of effluent limitations.

PHARMACEUTICALS
according to the
KLINE GUIDE TO THE CHEMICAL INDUSTRY (46)

Medicinals

Antibiotics
- Penicillins
- Tetracyclines

Vitamins
- B-complex
- E
- C
- A

Anti-infective agents
- Antiprotozoan agents
- Anthelmintics
- Sulfonamides
- Urinary antiseptics

Central depressants and stimulants
- Analgesics and antipyretics
- Barbiturates

Gastro-intestinal agents and therapeutic nutrients
- Choline chloride
- Amino acids and salts-b

Hormones and substitutes

Autonomic drugs
- Sympathomimetic

Antihistamines

Dermatological agents and local anesthetics
- Salicylic acid

Expectorants and mucolytic agents

Renal-acting and edema-reducing agents

Biologicals

Serums
Vaccines
Toxoids
Antigens

Botanicals

Morphine
Reserpine
Quinine
Curare
Some alkaloids
Some codeine, caffeine
Senna, aloe, podophullum, terpin

NFIC-D

Based on plant visits, discussion with industry representatives, and the literature review summarized in this report, NFIC-D further divided the SIC groups. Although the pharmaceutical industry can undoubtedly be classified in other ways, the NFIC-D categorization was useful in developing and applying effluent limitations.

Most bulk pharmaceutical manufacturing plants employ two major types of processes: fermentation and/or synthesis of organic chemicals. The characteristics of wastewaters from these two processes may be substantially different. Most plants are actually a combination of these two types, yielding the third category. The fourth and fifth categories are self-explanatory. The NFIC-D pharmaceutical industry classification follows:

*(1) Fermentation Plants -- Plants primarily employing fermentation processes to produce medicinals.

(2) Synthesized Organic Chemicals Plants -- Plants primarily engaged in the synthesis of organic medicinal chemicals (fine chemicals).

(3) Fermentation/Synthesized Organic Chemicals Plants -- Plants employing both fermentation and synthesized organic chemicals processes. Most moderate- to large-sized plants are in this category.

(4) Biologicals Production Plants -- Plants primarily engaged in the production of vaccines and antitoxins.

(5) Drug Mixing, Formulation and Preparation Plants -- Plants primarily engaged in the production of pharmaceutical preparations in final form, such as tablets, capsules, and solutions.

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* Parenthetic numbers reflecting industrial categories identify specific plants listed in Section I

A wide variety of products is made by pharmaceutical companies, and many of the products overlap into other fields. Such products include industrial chemicals, paints, plastics, fertilizers, pesticides. cosmetics, animal feed supplements, and ingredients used in candies, baked goods, cleaning agents, metal etching compounds, car radiator compounds and blueprints, just to mention a few. Product lists and technical description of many pharmaceutical ingredients are contained in these references: *Pharmaceuticals* (104), *Drugs in Current Use and New Drugs* (85), *Chemistry in the Economy* (116), *The Merck Index* (71).

IV. PROCESS DESCRIPTION

The unit processes used to produce pharmaceuticals are best categorized as fermentation, synthesized organic chemicals, biologicals, and drug formulation and preparation. However, this categorization is somewhat artificial since more than one series of processes is used in virtually all plants; for instance, fermentation is often combined with the production of synthesized organic chemicals. *Unit processes* are described below, followed by examples of *typical plant operations* which are considered both by category and products.

UNIT PROCESSES

Fermentation

The unit operations of fermentation are: seed production, fermentation (growth), chemical adjustment of broth, evaporation, filtration, and drying.

Seed Production

The seed culture is grown usually on a small scale and for a short time. Scale of seed production equipment approximates 5 to 10 percent of the size of the equipment used in the fermentation step. The seed can be used immediately or stored for use as required.

Fermentation

The seed is combined with an appropriate medium and allowed to incubate in agitated, constant-temperature fermentation vessels. The type of medium varies with the material to be produced, but typical mediums may contain one or more of glucose, soy meal, corn steep liquor, lactose, lime, and mineral salts.

Chemical Adjustment (Optional)

This step is required only if the final fermented material cannot be properly segregated from the medium at existing chemical conditions. Adjustment may occur in pH, conversion to a salt, addition of a solvent, or any number of these or other refinement techniques.

Evaporation (Optional)

In some cases, the fermentation product may be evaporated to concentrate the material.

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Filtration

A variety of filters are used to extract the desired product, including vacuum filters, filter presses and pressure filters.

Drying

Drying is used when the product is to be marketed as powders, tablets or capsules.

Synthesized Organic Chemicals

Because of the wide variety of chemicals produced, the unit processes involved in their synthesis vary. Generally, however, synthesis includes chemical reaction in vessels, solvent extraction (solid-liquid and/or liquid-liquid), crystallization, filtration, and drying. Any number of the steps can be used, combined in a wide variety of permutations. In some cases, the exact process is classified as company confidential.

Biologicals

To produce biological pharmaceuticals, specially prepared viruses and cultures of bacteria are injected into biological organisms such as eggs, horses, or other appropriate animals. The serum of interest is generally produced in a specific organ -- pancreas, blood, liver, etc. That organ is processed, and the raw serum is extracted and purified by evaporation, crystallization, filtration, and/or other purification steps. Increasingly, animals are used only for testing and organisms are being replaced by artificial mediums, such as beef broth. (Biological unit processes are not discussed in this report; however, for more detail see the Appendix, "Case History G, Wyeth Laboratories, Marietta, Pa.," a biologicals production and drug formulation plant.)

Drug Formulation

Drug formulation processes use standard steps of mixing (liquid or solid), pelletizing, encapsulating, and packaging. This processing is generally free of excessive wastes, which are therefore considered here only briefly.

TYPICAL PLANT OPERATIONS

Typical plant operations are discussed both by the dominant unit process employed and by the products produced.

FERMENTATION

In 1968, Lines discussed his experiences on fermentation wastes generated in Great Britain (10). He focused on the manufacture of antibiotics, such as penicillin and the tetracyclines, and vitamins, such as riboflavin (B_2) and cyanocobalamin (B_{12}).

Appropriate organisms are cultured in relatively complex nutrient solutions, stirred mechanically, and generally vigorously aerated. The desired crude product is removed from solution or from the cells of the organisms by solvent extraction, ion exchange, or absorption. A large proportion of the starting raw materials and cell material created during fermentation is disposed of as waste, or is partially recovered.

The particular strains of organisms are usually obtained when individual companies increase the productivity of previous organism strains by mutation and species selection. Otherwise, these strains may be acquired under license from other producers. Formulas for suitable fermentation mediums are likewise developed by the company or are purchased. Consequently, detailed information on fermentation processes and pharmaceutical plant manufacturing waste effluents is difficult to obtain.

Some data on starting fermentation solutions for antibiotics have been provided by Lines (10) as follows:

Benzyl penicillin	(g/l)	Bacitracin[a/]	(g/l)
Lactose	35	Starch	10
Glucose	10	Peanut meal	45
Corn Steep Liquor	35	Yeast	3
KH_2PO_4	4	Calcium acetate	0.5
$CaCO_3$	10	K_2HPO_4	1
Vegetable oil	2.5	$MgSO_4 \cdot H_2O$	0.2
		NaCl	0.01

[a/] Antibiotic from Bacillus subtilis

Other materials typically used in fermentation mediums are sugars, distillers' solubles, fish or whale solubles, soy bean meal, fish meal, molasses and trace minerals. Sugars, alkalis and organic acids may be added to the fermentation process to maintain levels of essential nutrients and desirable pH. Product yields, at least in the mid-1960's, were seldom more than 10 mg/l.

Vitamins

Four of the more important vitamins are manufactured by fermentation processes, including vitamin B_2 (riboflavin); vitamin B_{12} - from selected molds in fermentation vats; vitamin C (ascorbic acid) derived from sorbose - produced by a bacteria feeding on sorbitol, the latter prepared from corn sugar; and vitamin D - manufactured by ultraviolet irradiation of ergosterol (ergosterol represents a substance obtained from yeasts).

Vitamin B_2 (Riboflavin)

Riboflavin was discovered about 1933 and its chemical formula is $C_{17}H_{20}O_6N_4$. Riboflavin generally functions in the form of specific enzymes bound to certain proteins; a wide variety of human and animal body reactions depend on these protein systems. Riboflavin deficiency causes formation of oral, dermal and corneal lesions. Although riboflavin is widely distributed in plant and animal tissues, greater amounts are present in certain foods such as liver, milk, cheese, lean meats and leafy vegetables. Riboflavin is one of the many ingredients added to "enriched" flour, bread and various cereal products. It is added as a usual supplement to animal feeds to the extent of 2 to 8 g/ton feed; most goes into poultry and swine rations.

Manufactured both by chemical synthesis and microbiological fermentation, one-sixth of riboflavin in the U.S. as of the late 1960's was produced by fermentation. Most of the latter riboflavin was used in crude concentrates as animal feed supplements.

In fermentation, three groups of micro-organisms have been found to efficiently synthesize riboflavin: 1) bacteria of the butanol-acetone group, chiefly represented by Clostridium acetobutylicum; 2) selected Candida yeasts; and 3) two yeastlike fungi -- Eremothecium ashbyii and Ashbya gossypii.

Using C. acetobutylicum, various carbohydrate-containing mashes such as cereals, corn, rice, whey and semisynthetic starch materials have been used as appropriate media. Iron-sequestering agents are often added to these particular broths. The mash is generally incubated at 37 to 40°C (99 to 104°F) for 2 to 3 days. During fermentation, mixed ethyl alcohol, acetone and butanol vapors are commonly collected, condensed and fractionally distilled. The riboflavin may be recovered by absorption and elution, extraction with butanol followed by precipitation from the extract by petroleum ether, or addition of a reducing agent causing precipitation of the riboflavin.

When E. ashbyii is used in fermentation, the medium may include proteinaceous materials, carbohydrates and vegetable oil lipids. Fermentation is usually conducted for 50 to 90 hr, then the final beer is heated to free the riboflavin from the mycelium. This procedure has provided riboflavin yields of 500 μg/ml broth, although some reports indicate returns threefold greater (94).

At Dawes Laboratories in Newaygo, Mich. (92), the medium for riboflavin was dextrose, corn steep water and animal stick liquor. The organism used was Ashbya gossypii, a yeastlike fungus. Described as a whole-broth process, the entire spent fermentation mash was dried, eventually yielding a final feed supplement product rich in vitamin B_2.

Vitamin B_{12} (Cyanocobalamin)

Hester and Ward (92) in their 1954 report describe vitamin B_{12}, obtained almost exclusively from microbial sources either as a primary fermentation product or concurrently with certain antibiotics. The chemical formula for vitamin B_{12} is $C_{63}H_{90}O_{14}N_{14}PCo$. B_{12} is used in the treatment of pernicious anemia and nutritional deficiencies in humans, but the market for it is also extremely important in animal feed preparations. The amount of B_{12} necessary in a ton of feed is only a few milligrams. Furthermore feed-grade vitamin does not require the complicated purification processing as for human use. Merck in 1948 found that B_{12} could be produced by certain micro-organisms, notably those used in commercial production of streptomycin. Streptomyces olivaceus is one of the most promising of these organisms. Lederle Laboratories produces vitamin B_{12} simultaneously with Aureomycin (chlorotetracycline), using Streptomyces aureofaciens in fermentation.

Dawes Laboratories in Newaygo, Mich. (92), started producing vitamin B_{12} and vitamin B_2 in 1950. The organism used for vitamin B_{12} production was S. olivaceus, with a typical medium composition of distillers' solubles, dextrose, calcium carbonate and $CoCl_2 \cdot 6\ H_2O$. The seed fermenters were 1.5 m^3 (400 gal) vessels and the production fermenters were 20 m^3 (5,200 gal) tanks. Foaming of the aerated medium presented certain problems which were minimized by the addition of oils, such as corn oil, soybean oil, and lard oil, before cooking, and/or the addition of sterile oil during fermentation. The fermentation temperature was maintained at about 28°C (82°F). The cultures were grown in the seed tanks for about 2 days, and subsequently the production fermenters were operated from 3 to 5 days.

In the early 1950's, the fermentation broths were usually harvested when containing about 1.5 to 2.5 $\mu g\ B_{12}$ /ml of broth. Yields, however, have no doubt improved greatly since the 1950's. After fermentation, the active ingredient, vitamin B_{12}, is stabilized by reducing the pH to about 5.0 with sulfuric acid and adding sodium sulfite.

Vitamin B_{12} for animal feeds is a whole-broth concentration process. The Dawes Lab process involved drying the spent fermentation mash in an evaporator or vacuum pan. The resulting syrup was then fed into a double-drum dryer yielding a solid product with only about 5 percent moisture. The dried material in bulk was then passed through a hammer mill, a mixer, and eventually bagged or drummed as vitamin B_{12} feed supplement. The finished product assayed at 10 to 30 mg vitamin B_{12}/lb. The product also contained about 35 percent protein and appreciable quantities of niacin, pantothenic acid, pyridoxin, riboflavin and thiamin.

Dawes Labs and others in the 1950's were seeking a micro-organism capable of producing both vitamin B_{12} and a desirable antibiotic for dual incorporation into their animal feed supplements (92).

Vitamin C (Ascorbic Acid)

Vitamin C can be produced at a reasonable price by modification of the natural sugar, glucose, which provides a cheap and abundant starting material. The commercial synthesis is an interesting example of a combination of chemical manipulation together with the specific abilities of micro-organisms.

Glucose is reduced to the chemical sorbitol. Fermentation with Acetobacter suboxydans produces 1-sorbose. Further chemical reactions involving acid and alkalai additions produce ascorbic acid, which is recovered for use (116).

Citric Acid

In 1923, full-scale production of citric acid was initiated in the U. S. utilizing fermentation via the fungi, Aspergillus niger. Deep-tank fermentation with A. niger was introduced in 1952. As of about 1961, U.S. production of citric acid was 27 to 36 kkg (60 to 80 million lb) annually, practically all derived from fermentation. Citric acid has extremely widespread use. It is also the most extensively employed organic acid in the food industry (95).

In the early surface culture method of fermenting citric acid by A. niger from sugar solutions, beet sugar molasses derived from straight-house sugar factories constituted the best source of carbohydrate. After 6 to 12 days, the fermentation was terminated and the mycelium was washed and pressed to remove residual adhering citric acid.

The deep-tank or submerged fermentation process for citric acid was conducted at low pH's and ammonia could be added as a nutrient during fermentation. After 5 to 14 days, the mycelium was filtered off and the desirable citric acid was recovered.

Citric acid is recovered by either precipitation as the calcium salt, or by crystallization upon concentration of the filtrate. With the first method, the filtrate is heated to about 60°C (140°F) and calcium hydroxide is added. The precipitated calcium citrate is filtered out and washed thoroughly. The calcium citrate is acidulated with sulfuric acid giving filterable calcium sulfate. In the second method, dilute citric acid is purified by decolorization and demineralization, then subjected to evaporation. The mixture is centrifuged and the crystals are washed and dried.

When conditions have permitted, citric acid has been produced from lemons, generally the culls and low-quality fruit. Juices from shredding and pressing the fruit pulp are combined with washwaters and subsequently fermented by yeasts. The fermented juice with 3 to 4 percent citric acid is filtered and limed, giving calcium citrate. After it is filtered and washed, this product may be marketed as crude calcium citrate, or the citric acid may be recovered and purified by the steps described above (95).

Antibiotics

Penicillin

The Penicillium mold was nurtured by Fleming in London in 1928-29. A very small quantity of penicillin was extracted which was found extremely effective against Staphylococcus infections. However, mass production facilities were not available then. Florey and Chain of Oxford University directed new efforts toward working with Fleming's mold. Later they solicited U.S. pharmaceutical experience from Pfizer, Merck and Squibb toward full-scale production of penicillin vitally needed during World War II. Eventually Penicillium chrysogenum was developed which, under proper culture conditions, gave 200 times more penicillin than Fleming's Penicillium notatum. Full-scale production was achieved with fermentation procedures using corn steep liquors as the basic medium, and ample supplies of penicillin were finally available in the early 1940's (112).

In 1958, Ross (8) provided detailed criteria on antibiotic fermentation operations. In some of the earliest penicillin processes, yields as low as 30 to 60 IU/ml of broth were obtained. With submerged fermentation techniques using large fermenters, yields were eventually increased to 5,000 IU/ml and higher. Significant advances also occurred in developing mutant organism strains which served to decrease fermentation time and increase antibiotic yields.

The respective sizes of full-scale fermenters utilized in the late 1950's were generally 38 to 76 m^3 (10,000 to 20,000 gal), but some units were 189 m^3 (50,000 gal) or greater. A height to diameter ratio of 2 to 3:1 is generally employed. The operating volume is usually about three-quarters of the total volume available to allow for foaming. Seed fermenters were used in the size range of 1,100 to 1,900 1 (300 to 500 gal). Fermentation periods were about 90 hr. The type of nutrient broth is usually corn steep liquor, a byproduct of the cornstarch industry and previously a discard material. Peanut oil or equivalent is added to the fermenters to break the foam or at least keep it under control. Mechanical agitation is necessary and power rating on the agitators is generally from 0.8 to 1.0 hp/100 gal of fermenter capacity.

The principal difficulties in operating the fermentation process are maintaining a delicate balance between the desired growth microorganisms and other competing forms of growth such as wild yeasts and bacteria. The latter forms may be present in the nutrient materials, water, air, or on the surfaces of the fermenter, or pipelines. The undesirable organisms can affect the fermentation process significantly.

In the case of penicillin, many organisms produce penicillinase, an enzyme which destroys the penicillin. Contaminating organisms consume the nutrients in the broth, retarding antibiotic generation. Unwanted byproducts may not necessarily be harmful, but they could be extremely difficult to remove in the final recovery processes. Very stringent sterilization procedures are used in every fermentation step.

The penicillin fermentation broth leaving the fermenters is filtered to remove mycelium, and the active compound is recovered from the filtrate by solvent extraction (8).

In the early 1950's, Mann (32) and Gallagher et al. (65) reported on Bristol Laboratories at Syracuse, N.Y., which began penicillin fermentation soon after it was formed in 1943.

The mold penicillin notatum was grown on the surface of quiescent nutrient solution in flasks, bottles or trays. A standard practice was to use 1.9 l (2 qt) bottles and incubate them on their sides to obtain the greatest quantity of culture. In some plants, as many as 30,000 bottles were inoculated each day. The surface culture method was replaced by the submerged, deep-vat fermentation tank process in the 1940's. These fermentation vessels increased from 4.5 m^3 (1,200 gal) up to 114 m^3 (30,000 gal) or larger in the late 1940's and early 1950's.

Seed for the fermentation tanks is obtained daily from the laboratory where a master culture of the mold is kept in test tubes. From the master culture, larger quantities of the mold are grown in flasks and small fermenters, which in turn serve as seed source for the full-scale fermentation tanks. The fermentation vessels may be up to three stories tall, but in some cases they are horizontally arrayed.

To the fermenters are added corn steep liquor, lactose, lime and mineral salts mixed with water to form a medium which is sterilized with heat or steam before inoculation. The penicillin mold is added to the tanks and the medium is incubated near room temperature under intense agitation and aeration for about three days. During the 73 hr incubation the mold has excreted the desired chemical, which is subsequently refined and concentrated into the finished penicillin.

The fermentation broth is removed from the tank and the growths are inhibited with formaldehyde. The mold or mycelium is removed by passing the entire ferment liquor through vacuum filtration. The mycelium may be burned, buried, used as a fertilizer, or dried and mixed with animal feed. The filtered broth from fermentation is acidified and extracted with amyl acetate or other solvents. The solvent is separated from the medium by centrifugation, and the penicillin values are transferred to an aqueous buffered solution. The spent broth passes through a solvent recovery column, is neutralized with caustic, and then is sent to the plant sewer.

Finishing process operations include: filtration, extraction with further solvents, discard of the spent buffer solution, washing the filter solids, crystallization and drying of the penicillin crystals. All operations are conducted under sterile conditions.

Various tests are made on the product before FDA certification and release, including assay and pharmacological tests in rabbits and mice, the pyrogen test, and animal safety, sterility and toxicity tests.

At Wyeth Laboratories in West Chester, Pa., fermentation broths are made of corn steep liquor, lactose and mineral salts. After appropriate fermentation, the fungi mycelium is separated from the spent broth by vacuum filtration. The penicillin is extracted from the broth with a solvent such as amyl acetate in an acid solution. After retrieving the penicillin, the solvent is recovered by stripping for further reuse (4, 36, 50).

Terramycin

The Terramycin plant of Charles Pfizer, Inc. in Sandwich, Kent, England was reported to be Europe's largest plant for the production of antibiotics in the mid-1950's (41, 80). The antibiotic Terramycin (trademark for oxytetracycline), is generated via fermentation by Streptomyces rimosus. It is used in the treatment of more than 100 diseases including typhus, pneumonia, peritonitis and dysentery, and is also used as an animal feed supplement. It was reportedly discovered in 1949 by the laboratories of Charles Pfizer in the U.S. after successive screening of micro-organisms from thousands of soil samples collected world-wide. The Kent facilities were completed in Oct. 1954. Refining of the Terramycin is carried out at Pfizer's nearby pharmaceutical plant in Folkestone, England.

In the sterile area of the Kent plant, the master culture spores of Streptomyces rimosus are stored freeze-dried until needed. The first stage of Streptomyces multiplication occurs in small containers under strict aseptic conditions. Large quantities of the mold are needed to set up the fermentation medium. While the mold is multiplying, the medium for the large, full-scale fermenters is prepared. Initially, the medium is prepared in 7.6 m^3 (2,000 gal) tanks to which are added desirable nutrient salts. This nutrient medium is then batched with water and heated. From the media preparation room, this mass is pumped to the full-scale fermenters and sterilized with live steam. The mold is subsequently added to the large fermenters.

The main fermentation tanks are under pressure to preclude entry of airborne contamination. Large quantities of sterilized air are blown through the fermentation mixture while the contents of the tank are continuously agitated. The ongoing reaction generates considerable heat, and the fermenters are cooled by continuously circulating cool water to maintain a predetermined constant temperature in the tanks. Antifoam agents are added to the process. After a prescribed number of days, the fermentation process is considered complete, the useable food in the media having been consumed by the organisms. During the first day, the original molds may have increased more than 100-fold, concurrently expelling the product from which the antibiotic is later extracted.

The broth in the fermenters now contains the highly diluted and crude Terramycin, the spent molds, and the spent medium. The total broth passes from the fermenters to the clarification area where chemicals are added to promote coagulation of the mycelium (molds) and to aid subsequent filtration. The mycelium is removed by straining the fermentation broth through a Dorr-Oliver stainless steel rotary vacuum filter. The filtrate which contains the active Terramycin, is then subjected to various chemical additions and processing to produce the crude intermediate salt, Terramycin hydrochloride, inside pressure platen filter presses. After successive washing of this salt, the Terramycin hydrochloride is partially air-dried and milled before further purification.

Refining of the Terramycin hydrochloride is carried out in glass-lined reactor vessels. The intermediate salt is mixed with a solvent and decolorizing agents, and the solution is pumped through a platen frame filter. The insoluble matter is removed and a clear solution of salt is passed to a vacuum tank with steam ejectors for concentration of the dissolved solids. This concentrated solution passes into a glass-lined crystallizing vessel where first-stage Terramycin hydrochloride is precipitated. Centrifugation separates the hydrochloride from the mother liquors. The resulting hydrochloride is then redissolved, filtered clear, and recrystallized as the pure salt. After washing, the pure Terramycin hydrochloride is dried in vacuum ovens. The refined Terramycin at Kent is bright yellow. A batch-fractionating unit is available for solvent recovery.

Some of the final refining processes for Terramycin hydrochloride are carried out at the nearby Pfizer Folkestone plant. The products received there are incorporated into the desired forms for subsequent sale such as tablets, oral and nasal suspensions, intravenous and intramuscular solutions. Besides Terramycin, the Kent plant manufactures other antibiotics (41, 80).

Reeves (64) described the Pfizer program for 1947-50, from the discovery of Terramycin to the subsequent development of process operations that led to full-scale manufacturing. The first experimental process in 1950 extracted Terramycin from filtered broth using n-butanol, but it was difficult to properly distribute Terramycin between butanol and the fermentation broth. To enhance this distribution, ammonium salts were used. Ensuing development improved and enlarged these extraction and refining processes for Terramycin.

Capacity of the Pfizer fermenters in the 1950's varied from 8 m^3 (2,000 gal) for the pilot plant tanks in Brooklyn, N.Y. to 95 m^3 (25,000 gal) for some of the production fermenters at the Groton, Conn. plant.

The air supply for the fermenters passes through special filters for sterilization before being introduced through distributors at the bottom of the fermentation tanks.

When the fermenter has reached maximum activity after several days of incubation, the fermentation beer is removed and passed through continuous rotary precoat vacuum filters. The screened mycelium is sent through a drum dryer and the residues are recovered for use as animal feed supplements. The filtered beers are delivered to a treatment tank to which quarternary ammonium salts are also added. The solution is then passed through a second rotary vacuum filter. The filtrate containing the spent fermentation beers passes through evaporators and a spray drier for recovery of large amounts of material useable as animal feed supplements. The filter cake containing the Terramycin "Q" salt is recovered, dried by warm air in cabinet-type driers, and transferred to the refining operations.

Dried Terramycin Q salt is treated within glass-lined stirred reactors together with methanolic hydrochloric acid. The treated solution is routed through a series of filtering steps for removal of filter-aid and other insoluble products, and a crude grade of Terramycin hydrochloride is obtained. The final process steps designed to yield purified Terramycin hydrochloride involve solvent recovery, vacuum distillation, recrystallization, washing of the crystals, centrifuging, and a number of unknown steps. The bulk purified drug receives final drying in vacuum trays or equivalent equipment. The 8 m^3 (2,000 gal) fermenters, seeded with from 57 gm (2 oz) to 19 l (5 gal) of pure culture, were reported to yield about 4 kg (9 lb) of antibiotic in the early 1950's. Antibiotic production efficiency has undoubtedly increased tremendously up through the present. A high degree of solvent recovery should necessarily be integrated into the Terramycin refining processes (64).

Streptomycin

In 1958 Bartels (83) described the transition from laboratory to full-scale manufacturing of streptomycin, which resulted in development of the "Whole Broth Process." Streptomycin is produced by the Streptomyces species under favorable conditions of fermentation over a 4- or 5-day incubation.

Some of the first broth commercially produced contained less than 50 ppm of streptomycin. The early process involved acidification of the broth followed by filtering on pressure precoat filters. The antibiotic was absorbed from the clear, neutral filtrate by a carboxylic-type ion exchange resin. The resin was then eluted with dilute acid for recovery of the streptomycin, and this compound subsequently passed through a series of refining steps to obtain the pharmaceutical grade product. Although the yield of crude streptomycin in the broth was increased to more than 2,500 ppm, the concurrent filtration rates became extremely low, causing high filtering costs and considerable mechanical losses.

This led to the eventual development of the streptomycin whole broth ion exchange process. In this procedure, the mycelium is not filtered out before entering the ion exchange columns. Comparison of the whole broth process vs the original process is demonstrated as follows:

Parameter	Whole Broth Process	Mycelium Removal Process
	unit/g resin	
Activity of whole broth	320,000	320,000
Loss during pressure filtration	---	45,000
Activity of feed to resin column	320,000	275,000
Column loading (avg)	279,000	233,000
Percent column recovery, column eluate/feed	84.7	84.7
Percent overall recovery, column eluate/whole broth	84.7	72.9

Ross (8) described fermentation of streptomycin in the late 1950's. The respective fermenter designs and operating conditions were the same as those previously described for penicillin. The type of nutrient broth used was a mixture of soya meal and glucose in water, to which some metallic salts were added.

After fermentation, the streptomycin broth was acidified and required considerable filter aid for filtration. Streptomycin was recovered from the filtrate by adsorption onto charcoal or onto a cation exchange resin. Acidified alcohol was used as the eluate for charcoal and dilute acid for the resin. The eluate is further purified by passing a solution of streptomycin hydrochloride in 80 percent methanol through alumina or activated carbon (8).

Mudri and Phadke (7) described streptomycin production in 1968. A pure culture of Streptomyces griseus is subjected to aerobic fermentation within a medium of glucose and a nitrogen source (such as corn steep liquor). Following fermentation, the broth is filtered to remove the insoluble solids. The filtrate is absorbed on a resin or charcoal, and the active streptomycin is eluted by dilute acids from the charcoal or resin. The eluate is neutralized and concentrated under reduced pressure. The crude streptomycin product solution is then precipitated out by the addition of acetone and subsequently purified.

Enzymes

Enzymes, fundamental catalysts triggering specific chemical reactions without becoming a part of them, constitute one of the most unusual classes of substances produced by fermentation. Some of the more familiar of the enzymes are pepsin, ptyalin, and rennin which are digestive tract enzymes.

Enzymes are manufactured as commercial products for use in the brewing, meat packing, baking, cleaning, cheese making and the leather tanning industries. Examples are "Sure-Curd," a bacterial enzyme akin to rennin from animal stomachs, which is derived by fermentation for use in the cheese making industry; the bacterial enzyme, invertase, used in making candy with liquid centers; and amylase, an enzyme derived from molds and bacteria used for the conversion of starch into sugars. A number of bacterial enzymes are used in medicine to dissolve blood clots and destruct unwanted chemicals within the human body, particularly in sensitive individuals (112).

SYNTHESIZED ORGANIC CHEMICALS

Vitamins

Vitamin B_2 (Riboflavin)

Chemical synthesis of riboflavin (94) generally involves modifications and refinements of early Kuhn and Karrer reactions. Kuhn's procedure involved reaction of 6-nitro-3, 4-xylidine with d-ribose through a series of complex steps yielding riboflavin. The Karrer procedure increased the d-ribose-based yield and gave N-d-ribityl-3, 4-xylidine, an important intermediate for making riboflavin. Overall reactions in producing the intermediate include condensation, reduction, epimerism, and acetylation.

The intermediate can be condensed with violuric acid to give riboflavin, directly transformed through an azo-dye intermediate, then condensed or reduced to phenylenediamine, then chemically treated. All three procedures satisfactorily yield riboflavin.

Vitamin C (Ascorbic Acid)

In manufacturing vitamin C, the natural sugar glucose ($C_6H_{12}O_6$) is reduced to sorbitol ($C_6H_{14}O_6$), then is converted to sorbose ($C_6H_{12}O_6$) by the synthesizing capability of micro-organisms such as Acetobactor suboxydons. Further chemical modifications give the intermediate $C_6H_{10}O_7$, which when subjected to alkali and/or acid treatment is eventually converted to ascorbic acid.

Antibiotics

Chloromycetin (Chloramphenicol)

Chloromycetin (trademark for chloramphenicol), discovered in 1947, was one of the first of the so-called broad-spectrum medicinal antibiotics. The drug is efficacious against both gram-positive and gram-negative organisms. The compound is reported effective in combatting typhoid, paratyphoid, H. influenza, bacterial meningitides, and staphylococcal infections (96).

As of May 1952, the Parke-Davis and Co. plant in Hounslow, Great Britain was reported to be the only producer of an antibiotic by synthesis. Eleven reactions, subdivided into four main stages, constituted the basic operations (45).

The first three steps of the first stage, the initial condensation processes, are performed in glass-lined reaction vessels. Wide variation in solids content, viscosity and other characteristics create difficult agitation problems for this part of the operations. Three-point suspension stainless steel centrifuges are used for filtrations in this stage.

The second stage of the process uses stainless steel units and glass-lined refluxing units. Glass-lined steel vessels are used in acid hydrolysis. In the third stage of processing, stainless steel refluxing units and stainless steel reaction vessels are used.

Before reaching the final product, there are several drying operations. While a battery of drying ovens fulfills major drying needs, vacuum shelf driers are also available.

Since large quantities of solvents are necessary in the processes, extensive solvent recovery is on hand. Stills and fractionating columns are enclosed in the Hounslow plant. Due to the uncommon amounts of solvents and other flammable materials used inside the factory, fire design and precautions have received a great deal of attention.

The building has a comprehensive fume extraction system. All vessels are served by high velocity extraction ducts whereas the vacuum oven, shelf drier trays, centrifuge balance tanks and associated areas are served by fume hoods. The air extraction system has its own extraction fans and air washing equipment (45).

Chloromycetin was previously prepared from deep-tank submerged fermentation using various strains of the actinomycete, Streptomyces venezuelae. The fermented broth was extracted with amyl acetate, and the extract was concentrated, washed, and again concentrated. Crude crystals were filtered, dried and redissolved in hot water. The hot solution was decolorized, clarified and cooled to induce recrystallization. The purified crystals of chloramphenicol were filtered, washed, dried, pulverized, sieved and then packaged. This biochemical process scheme has now been largely replaced by organic synthesis (96).

The most commonly-used synthesis process starts with p-nitroacetophenone. The consecutive steps involve bromination in a variety of inert solvents, addition of a chlorinated solvent followed by alcoholic mineral acid hydrolysis, acetylation with acetic anhydride and alkali, the addition of formaldehyde in the presence of sodium bicarbonate, chemical reduction, acetylation, nitration with fuming nitric acid, acid hydrolysis, recovery of the d-base by precipitation with alkali, and finally acetylation of the dried base to give a good yield chloramphenicol (96).

Adinoff in 1953 (59) and Melcher in 1962 (13) provided data on process description and methods of waste treatment in the manufacture of synthetic Chloromycetin at the Parke-Davis plant in Holland, Mich.

The synthesis of Chloromycetin introduced at Holland, Mich. in the early to mid-1950's, was divided into eight major steps involving some 40 independent manufacturing procedures. The plant is at the mouth of the Black River and the head of Lake Macatawa. Treated waste discharges enter almost directly into the Lake which is used for swimming, boating, fishing, and service water for various other companies on the lake.

Sulfa Drugs

The sulfa drugs, or Sulfonamides, represent a very large group of compounds; several thousand derivatives have been synthesized. Sulfa drugs were the first drugs to control systemic bacterial disease, and today still have important application. Early studies in sulfa drugs led to the discovery of Prontosil, the first drug to cure bacterial septicemias (blood poisoning). Prontosil was found to quickly dissipate, and sulfanilamide was formed in the body. Activity of the drug was consequently attributed to sulfanilamide. Thereupon, extensive testing of thousands of sulfanilamide derivatives was conducted to find active compounds with a broader spectrum of action (98).

Sulfa drugs may be strictly defined as sulfonamides, derived from sulfanilamide. The chemical formula for sulfanilamide is $H_2NC_6H_4SO_2NH_2$. Sulfa drugs are antibacterial agents, but their action is bacteriostatic (growth of bacteria inhibited without destruction) rather than bactericidal (destruction of bacteria). Sulfa drugs are still considered prominent, even though they have been largely displaced by antibiotics. These drugs continue to provide a principal treatment of urinary-tract disease for which they are claimed to be less expensive and possibly superior by some physicians. Other specific applications include the treatment of fungus-related nocardiosis, rheumatic fever and ulcerative colitis. Although antibiotics have largely replaced sulfa drugs for treating human disease, this has been less true in animal therapy because of the relatively low cost of the sulfas. Sulfaquinoxaline and Sulfamethazine are important drugs used to combat coccidiosis in turkeys and chickens. Other prominent and typical sulfa drugs are sulfathiazole, sulfadiazine and sulfaguanidine.

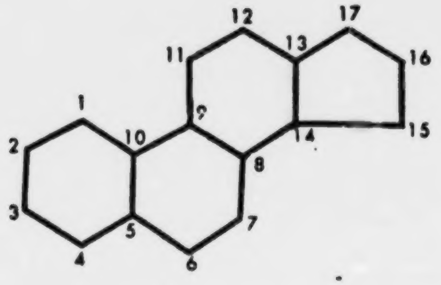
In the manufacture of sulfa drugs, acetylsulfanilyl chloride is usually reacted with the appropriate amine. Extra amine or a base is generally available to neutralize HCl made free within the reaction. The resulting acetyl product is then usually hydrolyzed with alkali to give the desired sulfanilamide derivative. Many variations are possible in these reactions, some of which may involve acetylation, diazotization, or amination. The sulfa drugs reached a maximum production of 4,536 kkg (10 million lb) annually in 1943 which dropped to less than half this amount in 1944 when antibiotics were commercially introduced. Since that time, the level of the sulfas has remained fairly constant. U. S. production of sulfa drugs and antibiotics is shown below (98).

Year Drug	1942		1943		1946		1952		1956		1966	
			(left col. = kkg)						(right col. = lb x 1,000)			
Total Sulfa Drugs	2,465	5,435	4,539	10,006	2,315	5,104	2,625	5,786	1,731	3,817	2,472	5,450
Sulfathiazole	723	1,594	--	--	915	2,016	328	724	∿ 0	∿ 0	∿ 0	∿ 0
Total Antibiotics	0	0	0	0	17	38	675	1,487	892	1,967	4,378	9,652
Penicillins	0	0	0	0	16	35	304	671	286	631	949	2,092

Steroids

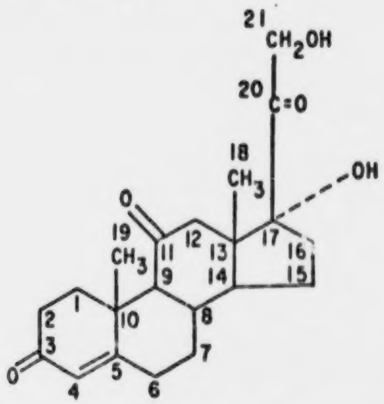
Steroids manufacturing as early as 1959 on a dollar volume basis was in second place among ethical pharmaceuticals, holding 24 percent of the $1.9 billion pharmaceuticals market, and outranked only by antibiotics (73). In 1958-1959, the anti-inflammatory steroids, mainly cortisone and related compounds, comprised 75 to 80 percent of the steroid market. The remainder of sales come from sex hormones used in treatment of endocrine disorders (i.e., glandular and other associated body organs). In the 1960's, the anabolic agents (those promoting tissue building functions and particularly important to the growing population of geriatric patients) were expected to lead the market gain for steroids. A very large market for steroid hormones capable of acting as contraceptive agents was also visualized at that time (73).

The major classes of steroids include the sterols, the bile acids, the adrenal cortical hormones, the sex hormones, various contraceptive drugs, insect molting hormones, cardiac-active lactones, sapogenins, certain alkaloids, and certain antibiotics. The basic steroid compound has three benzene groups together with a pentene group, constituting 17 available carbon positions as shown below:



The first important steroid, introduced into use in 1949, was cortisone. The beneficial action of cortisone as an anti-inflammatory agent was related to its ability in minimizing the inflammatory response of tissues to infective or toxic attack. Besides combating rheumatoid disease, cortisone preparations appeared to have great value in treating skin disorders, blood diseases, eye infections, and endocrine disorders.

Cortisone is chemically comprised of the four rings of the cyclopentanophenanthrene nucleus, depicted below. It has methyl groups at the C-10 and C-13 positions, a two-carbon side chain, the hydroxyl group at C-17, an oxygen atom at C-11, and a ketone at C-3 in conjunction with a double bond at the 4, 5 position.



Cortisone

The only production process available for cortisone in 1949 involved desoxycholic acid, a constituent of ox bile, as the base material for generating the steroid. Some 37 chemical steps were necessary to produce cortisone, with about 10 steps necessary to shift the oxygen from position 12 to 11. Clinical studies have shown there must be an oxygen in position 11 to have an active compound.

Complexity of the synthesis, relatively short supplies of ox bile, and low yields all limited the supply of cortisone and kept prices very high. Improvements in cortisone and other steroid production were sought, and a breakthrough was reported by Upjohn in 1952 (73).

Progesterone as an Intermediate to Cortisone

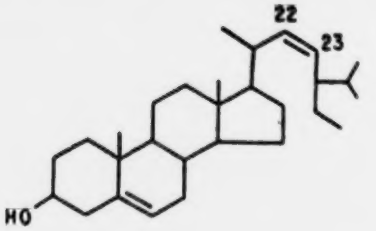
Upjohn Company. In 1952, Upjohn perfected introduction of an 11-hydroxy group into progesterone (female sex hormone) by utilizing Rhizopus arrhizus, a common mold. This was a microbiological oxygenation of steroids that meant a variety of starting materials could now be used to derive progesterone. This precursor material not only to cortisone but also many other active steroids is termed 11-hydroxyprogesterone.

At Upjohn, soybeans were a major starting material in producing soybean sterols, including stigmasterol. Stigmasterol in turn is synthesized to progesterone, which proceeds by microbiological oxygenation to the chain of various desired steroids. Soybean oil byproducts are prepared from soybeans, and from these byproducts is extracted a sterol mixture containing 12 to 25 percent stigmasterol, plus large amounts of mixed sitosterols. Unfortunately, since the physical properties of stigmasterol and sitosterols are nearly identical, the next problem was how to best separate these two types of sterols (73). The chemical configuration for stigmasterol is shown on the following page with the overall schematic for steroid production from soybeans.

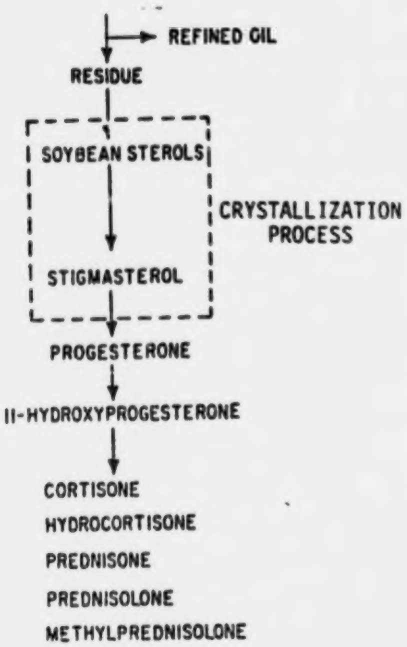
The older commercial process for separation of stigmasterol and sitosterols was quite time-consuming, expensive, and has low yields. Uphohn reported development of highly specialized procedures whereby stigmasterol could be selectively isolated in high yield and high purity from mixtures containing sitosterols and extraneous materials. These operations comprised multistage countercurrent crystallization using diverse selected solvents.

The Upjohn countercurrent crystallization process starts with soybean-derived feed solids containing about 20 percent stigmasterol. Through six successive crystallizations of this material, the final product is built up to 97 percent stigmasterol. Essentially, steady state conditions in the Upjohn process make it possible to achieve in excess of 85 percent of the total theoretically available stigmasterol in the feed solids (73). The solvent used in the Upjohn process is an azeotropic mixture of 63 percent ethylene dichloride and 37 percent n-heptane.

Pressure filtration is employed throughout all processing because of the handling of volatile solvents, the presence of flammable mixtures of air and solvent vapors, and the need to increase solvent recovery to the maximum extent practicable. A very high degree of solvent recovery is necessarily expected from the overall processing. The molten sterol



Stigmasterol


REFINED OIL
RESIDUE
SOYBEAN STEROLS
CRYSTALLIZATION PROCESS
STIGMASTEROL
PROGESTERONE
11-HYDROXYPROGESTERONE
CORTISONE
HYDROCORTISONE
PREDNISONE
PREDNISOLONE
METHYLPREDNISOLONE

Steroid production from soybeans

residue discard from the process containing about 2.8 percent stigmasterol (a black tarry liquid) is drained into large load-lugger truncated containers. In about 7 days the melt solidifies into a semicrystalline mass. The containers are discharged to outside storage or disposal by simply inverting the load-luggers. An alternative to casting the residues in pigs is to process this material for recovery of β-sitosterol, although again a discard is formed (73). Problems of solid waste disposal and associated leachability appear to merit critical attention.

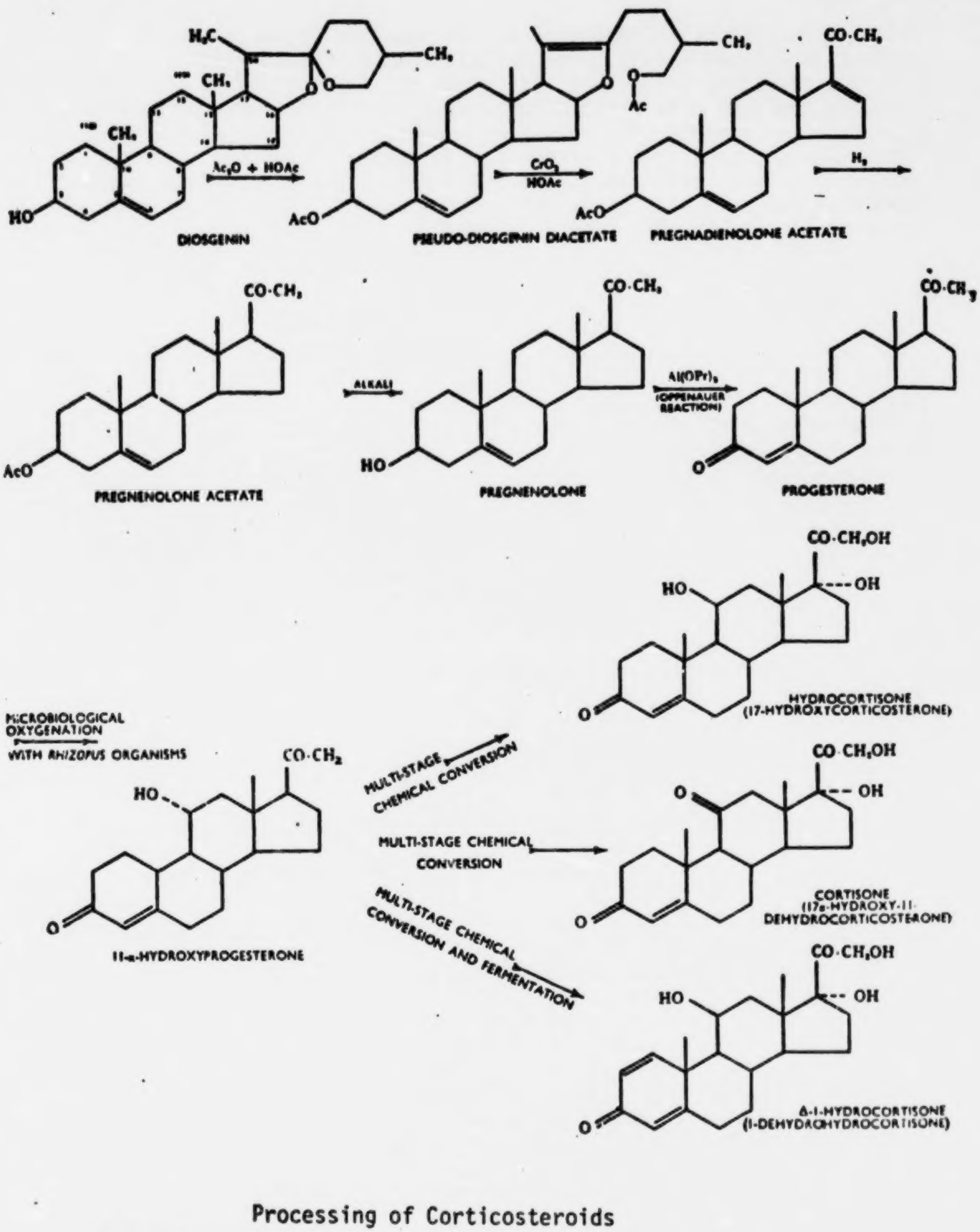
Boots Pure Drug Company. A close association was maintained in the 1950's between Boots Pure Drug Co. of Great Britain and the Upjohn Company in the U.S. From this association and continued research in Great Britain, Boots constructed a new plant at Beeston near Nottingham in 1955 for the preparation of cortisone, hydrocortisone, and α-1-hydrocortisone (40). The Beeston facilities included fine chemicals manufacturing plus fermentation, with full packaging capability.

The base production material was diosgenin, obtained from the wild vegetable Dioscorea, otherwise known as Testudinoria sylvatica, or elephant's foot, believed primarily obtained from South Africa. Essentially, diosgenin is converted to progesterone, an intermediate product, by a five-stage chemical process. Fermentation and microbiological oxygenation convert progesterone into 11-α-hydroxyprogesterone. This precursor is converted to the three end products of hydrocortisone, cortisone, and α-1-hydrocortisone via multistage chemical synthesis; however α-1-hydrocortisone requires an extra fermentation step for incorporation of an additional double bond into this compound. The latter chemical is reported to have greater steroidal activity and less undesirable side-effects (40).

The production of the three cortisone compounds requires from 10 to 30 steps, depending on the particular starting material and the specific synthesis. In contrast to the Upjohn process which employs stigmasterol from soybeans as the starting material, Boots Pure Drugs uses the plant extract, diosgenin. Both processes yield the intermediate product, progesterone, a female hormone. Formation of the important precursor 11-hydroxyprogesterone is conducted by fermentation using the mold Rhizopus arrhizus, which is apparently identical in the British and American processes. Boots Pure Drugs process operations are outlined in the figure on the following page.

Conversion of progesterone to the hydroxy form takes place in 15 m^3 (4,000 gal) stainless steel fermentation tanks and requires several days. The hydroxyprogesterone is precipitated in the fermenters in a finely dispersed form. The fermentation beers are removed and passed through a rotary vacuum filter for separation of the mycelium.

Extraction of 11-hydroxyprogesterone is necessary both from the aqueous fermentation broth and from the mycelium. The broth is extracted with a suitable solvent in a Podbielniak centrifugal extractor.


DIOSGENIN
Ac_2O + HOAc
PSEUDO-DIOSGENIN DIACETATE
CrO_3 HOAc
PREGNADIENOLONE ACETATE
H_2
PREGNENOLONE ACETATE
ALKALI
PREGNENOLONE
$Al(OPr)_3$ (OPPENAUER REACTION)
PROGESTERONE
MICROBIOLOGICAL OXYGENATION WITH RHIZOPUS ORGANISMS
11-α-HYDROXYPROGESTERONE
MULTI-STAGE CHEMICAL CONVERSION
MULTI-STAGE CHEMICAL CONVERSION
MULTI-STAGE CHEMICAL CONVERSION AND FERMENTATION
HYDROCORTISONE (17-HYDROXYCORTICOSTERONE)
CORTISONE (17α-HYDROXY-11-DEHYDROCORTICOSTERONE)
Δ-1-HYDROCORTISONE (1-DEHYDROHYDROCORTISONE)

Processing of Corticosteroids

Boots Pure Drug Co., Ltd., Nottingham, Great Britain

The process, starting with diosgenin, proceeds through the important intermediates of progesterone and 11-hydroxyprogesterone to yield three final steroid products: cortisone, hydrocortisone, and Δ-1-hydrocortisone, (40).

Hydroxyprogesterone is removed from the mycelium by agitation with solvent in a fixed vessel. The desired chemical is carried with the filtrate resulting from subsequent plate and frame filters. This filtrate is combined with the appropriate aqueous layer from the Podbielniak extractor and concentrated in a film evaporator equipped with distillation. The slurry from the evaporator is crystallized into a white powder, mainly 11-hydroxyprogesterone. Many items of standard chemical equipment are used with heavy reliance on Pfaudler glass-enamelled reaction vessels and Pyrex glass conveyance pipelines (40).

Prostglandins

In the past couple of years, the Prostglandins have been introduced to the medical field. Chemically, the prostglandin products are a family of 20-carbon unsaturated fatty acids. They are characterized by a five-membered carbon ring and two long side chains. One side chain is seven carbon atoms long and ends with a carboxyl group. The other chain is eight carbon atoms long with a hydroxyl group in the C-15 position. The synthesized prostglandins are intended to simulate compounds originally thought to be produced by the prostate gland in the body. The prostglandins are involved at the cellular level in regulating many bodily functions including gastric acid secretion, inflammation and vascular permeability, contraction and relaxation of smooth muscles, body temperature, food intake, and blood platelet aggregation (115).

The ability of the pharmaceutical companies to synthesize prostglandins has apparently outstripped the ability to understand what these compounds are, what they do, and their biological effects and implications. Clinical trials, animal testing and toxicological studies are being conducted in earnest. Only two prostglandins have so far reached the market for human use. The Upjohn Company distributes two naturally-occurring prostglandins, called E_2 and $F_{2\alpha}$ in Great Britain for inducing labor and for terminating pregnancy, respectively. In the United States, $F_{2\alpha}$ is available but only on a restricted basis.

Problems with prostglandins include their rather rapid metabolism in the body and the lack of tissue specificity. Whereas certain tissues may be properly impacted, at the same time the drug may adversely affect other tissues or organs. One of the more important syntheses for prostglandins is characterized by developing a γ-lactone fused to the 5-membered carbon ring at the C-8 and C-9 positions. The two side chains are added at a later stage in the synthesis. Natural sources of prostglandin have been found, such as the sea whip (a species of Caribbean coral) in the Cayman Islands, but commercial manufacture of prostglandins by the major pharmaceutical companies has been based upon total synthesis (115).

FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS

Filtration

Filtration techniques are extensively used in process operations but also may have application in pharmaceutical waste treatment. The absolute filter removes ultrafine particulate matter from final pharmaceutical products, such as liquids and intravenous solutions. Almost total elimination of particulate matter is feasible today. Apparently, contamination of the product due to settling of airborne particles in manufacturing is not a major problem compared with liquidborne contamination, as such may enter with deionized water or other sources.

Absolute vs Nominal Filters

Of the various filter types, only the wire mesh screen filter and membrane filter are considered absolute. These absolute filters have a pore-size rating (a definite largest particle that can penetrate the filter) which remains the same throughout the life of the filter. Both of these filters have a continous matrix, do not migrate or slough off, and rely solely on their pore size for particle retention.

When the solution to be filtered is nonaquaeous or contains a solvent incompatible with the filter, solvent-resistant membrane filters may be used. The most common membrane filter is the 1.5μ pore size. For fine particle removal, the 1.2μ pore-size membrane filter is frequently used. Therefore, all particles larger than 1.2μ in their maximum dimension will be removed, providing nearly complete protection from all contaminants.

In contrast to the absolute filters, depth-type filters have no definite pore-size rating. Because of their random orientations of substructures, they are rated on a nominal basis. They effectively remove gross matter, slimes, and sometimes even bacteria, but they do migrate. Generally, the ideal system is a combination of a large depth-type filter followed by an absolute filter (14).

Funda Filter

The Funda Filter is used for filtering, washing and drying such products as streptomycin and penicillin crystals, sorbite, salazopyrine, phenacetin, steroids, and intermediate chemicals for cortisone manufacturing. Also, it is used with activated carbon for filtering penicillin liquors either in the aqueous or solvent stages (26).

The Funda Filter is a vertical unit with a series of horizontal filter leaves enclosed by the filter vessel. Filtration takes place only on the upper surfaces of the horizontal leaves. Two forms of filter units are available. One, the precoat filter (or slurry discharge filter), is designed to discharge the separated filter cake as slurry at the end of the run. The other, a dry-residue filter, discharges the collected solids from the filter as a dry or semidry cake. Both forms of filters may or may not be precoated and incorporate filter aids. The filtering media is a fine metal screen or a cotton or synthetic cloth which retains particles 5μ or smaller. The dry residue filter becomes increasingly important because operating requirements today are specifying a dry cake discharge ready for disposal.

The filter vessel under pressure can be used as a reactor if necessary. It is particularly suitable for handling of volatile, toxic, explosive, or noxious materials that must be confined in a pressure vessel. It can be fully automated and instrumented. The collected cake can be washed with either water or solvent. The Funda Filter also can treat the residual heel left after filtration by completely disgorging the final tank liquids as clear filtrate. If warranted, the filter cake can be dried to any degree within the filter vessel. Centrifugal force and air or inert gas sparging can quickly and easily release the cake from the filter leaves and the vessel.

In straight filtration, if the filtrate is turbid, it may be recycled to the feed tank and again through the filter until it becomes clear. After filtration, washing the cake may involve relatively large or small amounts of wash liquid. A very expensive solvent used for washing would be limited in volume. Successive washings may be conducted with different wash liquids, each to dissolve specific materials in the cake - a process known as selective washing. Considering the variety of process operations in pharmaceutical manufacturing, the chemical values may be largely contained in the filter cake, or otherwise in the filtrates and within particular washes. But, the chemical values are generally in the liquid state. The filter discs need not be cleaned after each cycle, although cleaning is simple and requires little time.

Wastes associated with filtration include the discarded filter cake, wash liquids, precoat and filter aid materials, and washwater from filter cleaning (26).

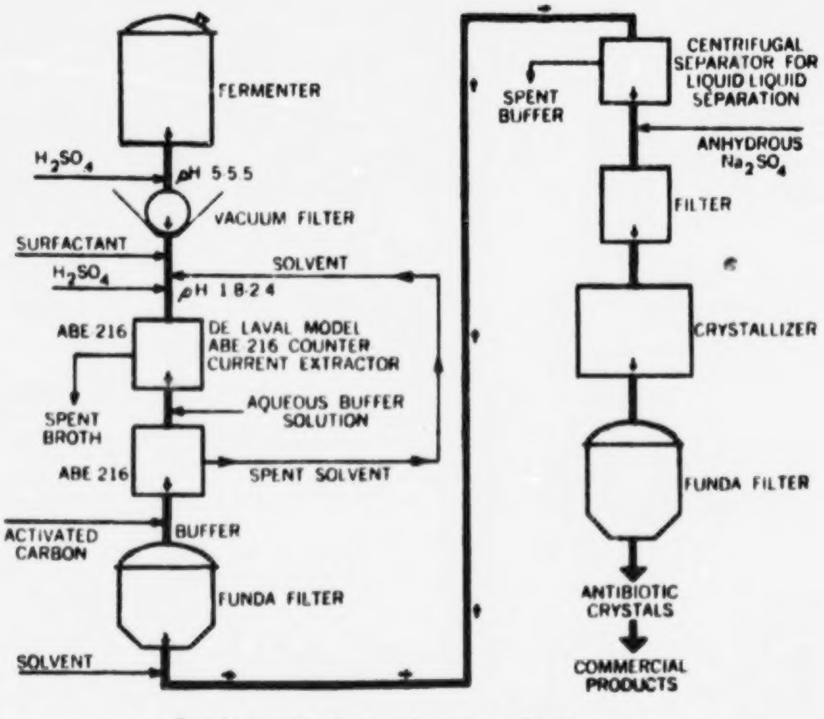
Specific Applications of the Funda Filter

In the manufacture of para-aminosalicyclic acid, bleaching and deodorizing with activated carbon is necessary and this process step is undertaken through the Funda Filter. A subsequent step in para-aminosalicyclic acid production involves the washing of these crystals inside the filter and then dissolving these solids for the next crystallization step. A third application is the filtration of the sodium salts from the para-aminosalicyclic acid which is followed by washing of the cake with alcohol and hot air drying inside the filter.

In the manufacture of carotene (a precursor of vitamin A), the Funda filter is used for decolorizing with activated carbon in more or less the same manner for para-aminosalicyclic acid above. The filter is used in some cases for the selective separation of alpha and beta-carotene using different solvents.

A pharmaceutical plant in England utilizes the Funda Filter for filtration of antibiotics in the solvent state and a second filter is used for recovery of the antibiotic crystals from the crystallizer. In another antibiotics production line shown below (Antibiotic A), the Funda Filter is an essential part of overall operations. The completed fermentation broth is adjusted with sulfuric acid and mycelium is recovered through a vacuum filter. To the antibiotic filtrate are added additional sulfuric acid, surfactants, and solvent. This mixture passes through a DeLaval Model ABE-216 countercurrent multistage extractor for the separation of spent broth, stripped solvent and an aqueous buffer solution carrying the active ingredient. Spent solvent is recycled to the filtered fermentation broth. Very high antibiotic recoveries are possible through the DeLaval unit.

The Funda Filter receives and filters the aqueous buffer solution containing the antibiotic values through activated carbon. A solvent is added to what is believed to be the filtrate, which subsequently passes through a centrifugal separator for separation of the spent buffer from the main process line. Anhydrous ammonia is added to the active liquid phase which is filtered before entering the crystallizer. The last stage employs a Funda Filter for final separation of the antibiotic crystals which are then ready for packaging (26). A number of waste lines are present which, however, are not shown on the figure.


FERMENTER
H_2SO_4
pH 5·5 5
VACUUM FILTER
SURFACTANT
SOLVENT
H_2SO_4
pH 1 8·2 4
ABE 216
DE LAVAL MODEL ABE 216 COUNTER CURRENT EXTRACTOR
SPENT BROTH
AQUEOUS BUFFER SOLUTION
ABE 216
SPENT SOLVENT
ACTIVATED CARBON
BUFFER
FUNDA FILTER
SOLVENT
SPENT BUFFER
CENTRIFUGAL SEPARATOR FOR LIQUID LIQUID SEPARATION
ANHYDROUS Na_2SO_4
FILTER
CRYSTALLIZER
FUNDA FILTER
ANTIBIOTIC CRYSTALS
COMMERCIAL PRODUCTS

Antibiotic A production (26)

DRUG FORMULATION

The Folkestone plant of Charles Pfizer and Company in Great Britain receives Terramycin hydrochloride and various other bulk pharmaceuticals and prepares and formulates these drugs into the desired form for customer sales. The Terramycin salt, upon reaching Folkestone, is first blended with additives to stabilize the product and also pH adjustment is made (41, 80).

All vials and bottles for antibiotics are washed and sterilized in a separate department. Two washing machines are available, one a single jet unit capable of handling 2,500 bottles/hr, and the other a multijet unit handling 8,000 vials/hr. Sterilized containers are kept within a sterile area which is under pressure to prevent entry of other than carefully controlled air supply. Air to the sterile area is dried to low relative humidity, cooled, and joins with recirculated air, the latter having passed through a cyclone and filters. This combined air passes through electrostatic precipitators, filters and glass wool before entering the sterile area. Washed rubber stoppers and clothing enter the sterile area via a steam autoclave. All filling of bottles and vials is conducted in the sterile atmosphere.

In the tablet manufacturing department, a binding agent and a disintegrant are mixed with the Terramycin, and the powder mixture is made into slugs. These are passed through a rotary granulator, next through a sifter, and then fed into a rotary tablet-forming machine. The tablets subsequently receive finishing coatings of shellac varnish, gelatin, white sugar and a wax polish. Other operations at the Folkestone plant include filling capsules, and the preparation of sterile and non-sterile liquid solutions, non-sterile powders, and various ointments (80).

V. WASTE CHARACTERISTICS

Major types of wastes from the pharmaceutical industry result from the process of *fermentation* or the production of *synthesized organic chemicals* and *biologicals*.

Process waste streams from *fermentation*, which produces antibiotics, vitamins, steroids and associated products, may include:

1. Liquid and solid wastes from fermentation operations
2. Liquid wastes from extraction and purification processes
3. Liquid and solid wastes from recovery processes
4. Floor and equipment washdowns
5. Sanitary and miscellaneous waste streams.

The strength of fermentation wastes can vary appreciably with different batches and between different manufacturers. Howe (6) estimates that the production of 0.45 kg (1 lb) of antibiotics generates from 11.4 to 13.2 m^3 (3,000 to 3,500 gal) of wastewater. Based on 4,540 kg (10,000 lb) of antibiotics produced daily during 1958, the average wastewater volume from antibiotics was 114,000 to 132,000 m^3/day (30 to 35 mgd). The concentration of pollutants in the washwaters depends on the extent of washing and the particular cleanup procedures employed.

Wastewaters from the manufacture of *synthesized organic chemicals* consist of complex mixtures of organic and inorganic materials having varied characteristics. The organic wastes include solvents, salts, acids and some plant and animal derivatives. These wastes usually contain high COD and TDS. The pH is usually very low or high and frequently the wastes are colored. The chemical derivatives extracted from natural plants or animal organs are unusually strong in TS, TSS, BOD and pH, and they are generally toxic to fish, aquatic life and animals. With careful production scheduling and waste stream control, it is possible to segregate the waste sources and separately treat the strongest or most complex chemical waste streams.

Biological pharmaceuticals production, including antitoxins, antisera and other associated compounds used in the treatment and prevention of specific diseases, results in the generation of large quantities of wastewaters which are difficult to handle. Such wastes contain animal droppings, animal carcasses and organs, blood, body fluids, fats, egg fluid, egg shells, biological culture media, feathers, solvents, antiseptic chemicals and herbicidal compounds. They are generally characterized by high BOD, COD, TS, toxicity, colloidal solids, color and odor. Sometimes the antitoxin and antisera wastes contain highly dangerous pathogens together with toxic components such as benzene, phenols, cresols, mercury compounds and a variety of other bactericidal materials. The presence of these compounds can cause great difficulty in determining waste characteristics by standard analytical methods (6).

The following data on waste characteristics of the pharmaceutical industry were reported for fermentation, synthesized organic chemicals, and biological plants.

FERMENTATION

The Upjohn Company, Kalamazoo, Michigan

The Upjohn Company (43) in the late 1950's and early 1960's analyzed spent beer wastes, defined as the end product after the extraction of either antibiotics or steroids. After solvent extraction, significant amounts of solvent and the antibiotic or steroid may still remain in the colored, odorous spent beers. Composition of the spent beers is as follows:

Component	Content
Total solids	1 to 5%
Ammonia-N	100 to 250 mg/l
BOD	5,000 to 20,000 mg/l
pH	3 to 7

Makeup of the total spent solids is typically:

Component	Content (%)
Protein	15 to 40
Fat	1 to 2
Fiber	1 to 6
Ash	5 to 35 (which includes Ca, P and K)
Total Carbohydrates	5 to 27
Steroid(s)	Present
Antibiotic(s)	Present

The vitamin content of the beer solids is given as:

Component	Content (μg/g)
Thiamine	4 to 12
Riboflavin (B_2)	10 to 150
Calcium	35 to 2,000
Pyridoxine HCl	125 to 75
B_{12}	Present
Folic acid	1 to 5

Howe (6) reports that spent fermentation broth solids can (potentially) amount to 0.2 kg (0.4 lb) solids per gallon of broth. This is equivalent to about 47,000 mg/l or 4.7 percent waste total solids. These solids, mostly dissolved, are characterized as high in nitrogen, phosphates, vitamins and may contain trace amounts of antibiotics. Howe emphasizes recovery of these solids, particularly for animal feeds.

Bristol Laboratories, Syracuse, New York

Bristol Laboratories (32, 65) analyzed penicillin production wastes which were a mixture of solids, spent broth, chemicals, waste acids and caustics, unrecovered solvents, and washing and cooling waters. The solid penicillin growth, or mycelium, is reported to have a high nitrogen and BOD content. The spent penicillin broth contains sugars, proteins and organic acids and is quite high in BOD and suspended solids. Depending on the amount of food remaining at the completion of fermentation, and the extent of in-plant control and recovery of solvents and mycelia, the spent broth will have a BOD ranging from 4,000 to 13,000 mg/l. In addition to day-to-day wastes, the disposal of contaminated fermentation batches presents a special problem since individual batches may run as high as 30,000 mg/l in BOD and 20,000 mg/l in TSS.

About mid-1948, before waste control procedures were fully implemented at Bristol Laboratories, the total wastes from the fermentation facility had a BOD population equivalent from 0.1 to 0.3 PE/l (0.37 to 1.0 PE/gal) of discharge, averaging 0.2 PE/l (0.74 PE/gal) waste. By controlling contaminated or spoiled fermentation batches and with improved control and recovery of solvents, these BOD loads were reduced 61 percent to 0.04 to 0.11 PE/l (0.16 to 0.43 PE/gal) of discharge, averaging 0.08 PE/l (0.29 PE/gal). After passing through equalization and partial neutralization (pH adjustment up to 4.5) the wastes were directed to municipal treatment.

In their early experiences, personnel at the Syracuse, N.Y. municipal treatment works recorded 35,000 mg/l BOD and TSS in the pharmaceutical plant penicillin sewer. These extreme values occurred before Bristol Laboratories initiated mycelium recovery and solvent stripping. BOD and TSS concentrations were later reduced to 5,000 and 3,000 mg/l, respectively. The strength of penicillin wastes can vary appreciably with different batches and from one manufacturer to another.

Impact on the municipal treatment plant appeared to be caused more by the quantity rather than the strength and nature of the wastes received from the Bristol Laboratories. The main effects were:

1. Solvents imposed additional loads on aeration units with greater costs for air supply
2. Rates were higher for recirculation of return sludge and other flows to reduce shock loads
3. Considerably larger volumes of sludge were produced as a result of the penicillin wastes. Much higher solids loads were subsequently imposed upon the digesters.

It was concluded that penicillin wastes are amenable to aerobic and anaerobic treatment, provided no substances are present which may poison or retard biological activity. However, over the years a greater than normal number of upsets, some serious, have apparently occurred at the Syracuse, N.Y., biological treatment facilities.

A Pharmaceutical Plant in India

Waste characterization data was obtained from a pharmaceutical plant producing penicillin and streptomycin (7). In penicillin production, molds of the Penicillium notatum-chrysogenum group are cultured in a medium of corn steep liquor, peanut meal, lactose and mineral salts. The wastewaters include mycelium and the spent filtrate and wash waters from succeeding steps. In streptomycin production, pure cultures of Streptomyces griseus are cultured in a medium consisting of a sugar source (glucose) and a nitrogen source (corn steep liquor or equivalent). The filtrate is absorbed on charcoal or a resin and the active ingredient is eluted from the resin with acid. The eluate is neutralized and concentrated. Acetone is used to precipitate the crude product which is purified in subsequent process steps. Streptomycin wastewaters also included mycelium and the spent filtrates and washwaters. Certain amounts of mycelium were sold as manure or stock feed.

Representative raw wastewaters were collected from the penicillin and streptomycin production areas. The average results of eight 24 hr composite samples and results based upon eleven grab samples are given in Table V-1. The streptomycin wastes were stronger than those originating from penicillin production. The nitrogen concentration was low but the phosphate, sulfate and chloride values were high. More than 40 percent of the total solids were volatile solids, indicating high biodegradability potential.

Reference was made to information previously reported by Muss in 1951 which showed combined wastes from penicillin manufacturing as having an average BOD of 2,100 mg/l, a variation in BOD from 750 to 5,000 mg/l, and total solids about 5,000 mg/l. Heukelekian reported an average of 4,475 mg/l BOD for penicillin wastes with a variation from 2,400 to 8,150 mg/l BOD. Spent streptomycin broth was shown to have an average BOD of 2,450 mg/l with a range in BOD values from 825 to 5,900 mg/l.

Antibiotic Wastes, Great Britain

Lines (10) describes fermentation wastewaters as being contaminated with solvents, disinfectants and various solids including filter aids. If the fermentation broths and mycelia can be evaporated and dried into salable end products, then the waste sources can be reduced to evaporator condensates and washwaters. The highly organic nature of fermentation waste creates a favorable situation for biological treatment, but treatment plant biota can be adversely affected by the antibiotic residues. The BOD of fermentation wastewaters is usually in the range of 5,000 to 30,000 mg/l. Analysis of a principal antibiotic waste in Great Britain preceeding recovery and treatment is depicted below:

Table V-1

Penicillin and Streptomycin Raw Wastewaters
Fermentation Plant in India (7)

Parameter	24-Hour Composites		Grab Samples	
	Penicillin Wastes	Streptomycin Wastes	Penicillin Wastes	Streptomycin Wastes
Color	Colorless	Pale yellow	--	--
Odor	Fruity	Septic	--	--
pH	6.3	6.2	3.9 to 7.8	2.9 to 8.7
	(mg/l)			
BOD (37°C; 99°F)	1,490	1,800	650 to 5,500	500 to 2,800
Total free and albuminoid ammonia (N)	17.7	31.0	3.1 to 29.4	3.0 to 57.1
Organic nitrogen (N)	17.3	29.1	0.8 to 35.3	7.8 to 40.9
Nitrates (N)	0.3	0.7	0.1 to 0.5	0.0 to 0.8
Phosphates (PO_4)	72.0	65.0	18 to 700	9 to 700
Sulfates (SO_4)	51.0	52.0	26 to 192	25 to 765
Chlorides	91.0	204.0	16 to 200	66 to 1,200
TS	1,910	3,590	480 to 26,200	960 to 4,950
TVS	880	1,450	200 to 12,180	480 to 3,070
TSS	420	1,750	70 to 1,080	80 to 1,800
Settleable solids, ml/l	8.0	81.0	2.0 to 56	2.3 to 214

Component	Content (mg/l except pH)
pH	9.3
TS	23,690
TSS	18
BOD	7,120
Total nitrogen (N)	1,260
NO_3(N)	41

SYNTHESIZED ORGANIC CHEMICALS

Squibb and Sons, Inc., Humacao, Puerto Rico

Squibb conducted treatability studies (about 1969-70) prior to construction of its integrated pharmaceutical plants in Humacao, Puerto Rico (23). Synthetic penicillin was to be produced at one plant, and two antifungals, Amphotericin and Mycostatin, at the other. Major unit operations consisted of hydrolysis, solvent washing, solvent recovery, crystallization, distillation and filtration.

Initial studies showed that wastewaters should be segregated into:

1. A strong process wastewater stream
2. A weak process waste stream together with methanol solvent recovery still bottoms, plus sanitary sewage
3. Service waters, which included boiler and cooling tower blowdowns and spent demineralizer regenerants.

The Squibb report emphasized that none of the dilute process wastewaters, including the methanol solvent recovery still bottoms, showed any sign of acute toxicity although no data were presented in this direction.

The proposed waste treatment and raw wastewater characteristics are given in Table V-2.

Berkeley Chemicals Division, Summit, New Jersey

Berkeley Chemicals Division (58, 102) produced various synthesized organic chemicals which were not specifically named. Raw materials and/or final products included sodium formate, formaldehyde, isopropyl alcohol, citric acid, dehydroxynapthelene sulfonic acid, cupric acetate, and xylol. Process wastes amounting to 94 to 190 m^3/day (25,000 to 50,000 gpd) and containing 8,000 to 20,000 mg/l BOD were trucked from the

Table V-2

Proposed Pharmaceutical Wastewater Treatment and Characteristics
Squibb and Sons, Inc., Humacao, Puerto Rico (23)

Stream	Treatment	Flow		BOD[a]			COD[a]		
		(m^3/day)	(gpd)	(kg/day)	(lb/day)	(mg/l[b])	(kg/day)	(lb/day)	(mg/l[b])
(1) Strong Process	Incineration								
avg		44.7	11,800	21,500	47,300	480,000	30,700	67,600	687,000
max		65.9	17,400	33,700	74,200		48,000	105,800	
(2) Dilute Process	Biological								
avg		127.9	33,800	82	180	640	113	250	890
max		141.6	37,400	86	190		127	280	
(3) Service Water	Neutralization and Settling								
avg		133.6	35,300						
max									
Composite		306.2	80,900	21,500	47,500		30,800	67,850	

[a] COD/BOD ratio of 1.4 assumed

[b] Calculated

plant and bled into the Summit, N.J. sewerage system. These wastes in 1962-63 were rated around 2,360 kg (5,200 lb) BOD/day mainly derived from spent mother liquors and equipment and floor washings. Cooling waters and condenser waters, relatively uncontaminated, were discharged untreated to the Passaic River.

Process wastes from five major sectors in the plant were described as:

Waste A -	Sodium formate, formaldehyde, hexaldehyde; 1,510 to 1,890 l/day (400 to 500 gpd) mother liquors.
Waste B -	Solutions from urea and decomposition products; 227 kg (500 lb) urea discharged/day.
Waste C -	Isopropyl alcohol, citric acid.
Waste D -	Waste from purification of dehydroxynapthelene sulfonic acid; becomes deep red when combined with iron.
Waste E -	Cupric acetate and xylol.

Overall process waste characteristics were given as:

Component	Content
Flow	94.6 to 189 m^3/day (0.025 to 0.05 mgd)
BOD	8,000 to 20,000 mg/l
Phenolics	5 to 500 mg/l
TSS	350 to 850 mg/l
VSS	70 to 85% of TSS
pH	8.2 to 10.1

Various laboratory and pilot plant studies were conducted on pretreatment of the chemical wastes. An effort was made to segregate the strongest waste streams to determine if separate treatment were justified. The following analyses were obtained:

Source	BOD		
	mg/l	kg/day	lb/day
Still bottoms No. 1	840,000	38	85
Still bottoms No. 2	166,000	36	80
Mother Liquor No. 1	27,700	351	775
Mother Liquor No. 2	27,000	340	750
Mother Liquor No. 3	20,000	254	560

The BOD load in the three spent mother liquor streams amounted to 946 kg (2,100 lb) BOD/day, representing about 40 percent of the total BOD load from the pharmaceutical plant.

It was difficult to determine BOD analyses for the process wastewaters. Using the BOD dilution techniques, a sliding BOD scale was evident in the various samples. BOD values increased with increasing dilutions, indicating a striking inhibitory effect. In a series dilution of the combined process wastewaters (using manometric techniques) ranging from 1 through 100 percent waste concentration, the BOD_7 of the pure waste was recorded as 600 mg/l, whereas the 1 percent waste (corrected to the 100 percent level) gave a BOD_7 of 13,000 mg/l. The latter value was more than 20 times greater than the former. For BOD results collected during the study, the reference author indicates it is very likely that maximum (desired) BOD values were not recorded.

The wastewaters were extremely strong and inhibitory to biological treatment. It was noted over the two years of study that not only did the overall plant BOD load increase from 1,810 to 2,720 kg (4,000 to 6,000 lb)/day, but also the character of the wastes was constantly changing.

Parke-Davis and Co., Holland, Michigan

As a first step in waste characterization and treatment facility planning at the Parke-Davis Chloromycetin plant in the 1950's, Company personnel studied each operation, the various reactions, chemicals used, respective yields, unreacted compounds, wastes resulting from the washing of solids during filtering operations, solvent recovery possibilities, byproducts, and auxiliary data (50). All wastes to be disposed of were listed, and a program was set up for testing the major wastes. These tests included pH, BOD, TSS and TDS, solvent content, toxicity, color and chlorine demand of the wastes.

The most deleterious wastes were defined as:

1. Bottoms from the solvent recovery plant
2. Wash "A" from one of the filtering operations
3. Wash "P" from another filtering operation
4. Filter and spent wash stream termed liquor "S."

Analysis on the composite of these four waste streams, consisting of 52.9 percent bottoms, 30.1 percent wash "A," 7.5 percent wash "P," and 9.5 percent liquor "S," was as follows (59):

Component	Content
pH	3.7
BOD (20-day)	45,000 mg/l
TDS	60,000 mg/l
Color	Reddish-brown; 12,000 units
Toxicity	2 to 5%

The wastes were said to contain complex, unidentified organic compounds resulting from the processes. Ions present included sodium, chloride, ammonium, acetate, bromide and nitrates. No flow values for the chemical waste system were reported. Chemical wastes were treated within the chemical process sectors for the removal of aluminum salts, sulfates, phosphates and immiscible solvents (13). The types of waste materials remaining in the chemical waste sewer were reported as:

Component	Content	
	(kg/day)	(lb/day)
Acetic acid	910	2,000
Ammonium acetate	910	2,000
Sodium acetate	770	1,700
Sodium chloride	450	1,000
Sodium and ammonium bromide	230	500
pH		4 to 5
COD		40 to 60,000 mg/l but sometimes as high as 100,000 mg/l
Large quantities of methanol, misc. tars and dissolved organics, xylene		

The various in-plant procedures required for removal of aluminum salts, sulfates and phosphates were sometimes more extensive than the chemical process steps that produced these compounds.

As the chemical wastes pass through retention-equalization tanks, some precipitates are settled out. Xylene formed an emulsion on the top of the retention tank, and was periodically skimmed off. The separated waste materials were trucked away to land disposal.

M/s Indian Drugs and Pharmaceutical Plant, Hyderabad, India

Preliminary production figures projected in 1962 for the various chemicals to be manufactured at the Hyderabad plant are shown in Table V-3. The groups of synthetic drugs include the sulfanilamides, the antipyretics, (i.e., phenacetin), the vitamins B_1, B_2 and folic acid, and the antitubercular drug, isonicotinic acid hydrazide. Large quantities of both inorganic and organic basic chemicals are necessary for intermediate chemicals production. Some slight shifting of product mix was indicated between 1962 and 1970. Patil (30) lists 35 chemicals to be manufactured whereas Mohanrao (54) later cites up to 70 various chemicals associated with the Hyderabad production facilities.

The Russians estimated that about 600 m^3/day (0.15 mgd) industrial wastewaters could be expected from the factory, excluding the sanitary sewage and the spent cooling and condenser waters. Waste constituents consist largely of inorganic and organic salts, almost all of which are dissolved. Approximate composition of the untreated synthetic drug wastes are given below (30):

Parameter	Concentration (mg/l)
Calcium chloride	600-700
Sodium chloride	1,500-2,500
Ammonium sulfate	15,000-20,000
Calcium sulfate	800-21,000
Sodium sulfate	800-10,000
Sulfanilic acid and related products	800-1,000
Various sulfa drugs	400-700
p-amino phenol, p-nitrophenolate, p-nitrochlorobenzene, etc.	150-200
Amino-nitrozo amino-benzene antipyrene sulfate	170-200
Analogous substances	150-200
Alcohols (methyl, ethyl, isopropyl, etc.)	2,500-3,000
Benzene, toluene, etc.	400-700
Chlorinated solvents (dichloroethylene, chloroform, etc.)	600-700
Other substances	Unknown

The M/s Indian Drugs and Pharmaceuticals installation, completed in the early 1970's, consisted of twelve blocks or sectors (54). Nine of these were to be used for the manufacturing of drugs and chemicals, and the remaining three for storage of raw materials, intermediates and final products. The nature and volumes of wastes discharged from each sector are shown in Table V-4.

The majority of wastes discharged are acidic. Sector 8, which produces intermediates for the manufacture of synthetic drugs, contributes slightly more than one-half of the concentrated industrial wastewaters from the factory. Wastes from Sectors 3 and 8 and the

Table V-3

Design Production, Synthetic Drugs and Intermediates (1962)
M/s Indian Drugs and Pharmaceutical Plant (30)
Hyderabad, India

Drug	Annual Production	
	(metric tons)	(tons)
Sulfadimidine	181	200
Sulfadiazine	136	150
Sulfaquanidine	68	75
Sulfacetamide sodium	45	50
Acetozolamide	23	25
Sulfanilamide	45	50
Urosulphan	23	25
Ethazol (Globucid)	23	25
H.N.H.	18	20
Chloroquin	4.5	5
Luminal	9	10
Phenacetin	91	100
Ditrazine	9	10
Pyramidone	36	40
Novalgin	9	10
Piperazine sulphate	9	10
Vitamin B-1	23	25
Vitamin B-2	2	2
Vitamin PP (nicotinamide)	27	30
Folic acid	.9	1
Total tons/year	782	863
(Intermediates)		
Acetanilide Sulphonylchloride	1,360	1,500
Acetyl acetone	91	100
Aceto acetic ester	45	50
Aceto propylic alcohol	45	50
Phyenyl ethylnalonic ester	18	20
Sodium bisulfite (38% soln.)	544	600
Dichloroethylene	272	300
Propionyl chloride	18	20
Ortho-formic ester	18	20
Hydrazine sulfate	181	200
Diethylamine	36	40
Sulfanilamide tech.	408	450
Beta picoline, purified	27	30
Gamma picoline, purified	18	20
Piperazine hydrate	36	40
Total tons/year	3,117	3,490

Table V-4

Character of Industrial Wastewaters From Various Sectors of the Hyderabad, India Plant, 1970 (54)

Sector	Activity	Wastes						Total Wastes	
		Acid		Alkaline		Neutral			
		(m^3/day)	(gpd)	(m^3/day)	(gpd)	(m^3/day)	(gpd)	(m^3/day)	(gpd)
1	Sulfa	28	7,400	33	8,720	0	0	61	16,100
2	Vitamin B_1	7	1,850	4.2	1,110	15	3,960	26.2	6,920
3	Vitamin B_2 and folic acid	4	1,060	3	790	10	2,640	17	4,490
4	Antipyretic and antitubercular drugs	15	3,960	18	4,760	23	6,080	56	14,800
5	Products using sodium metal	5.5	1,450	8	2,110	28	7,400	41.5	11,000
6	Sodium bisulfite	1	260	0	0	0	0	1	260
7	Phosgenation and chlorination	8.5	2,240	0.3	80	0	0	8.8	2,320
8	Intermediate chemicals	262	69,200	45	11,900	0	0	307	81,100
9	Pilot plant and central laboratory	6	1,590	4	1,060	20	5,280	30	7,920
12	Liquids and solids chemical storage	0	0	0	0	0.1	26	0.1	26
13	Acid and alkali storage	15	3,960	0.1	26	0	0	15.1	3,990
14	Raw materials	0	0	1.5	400	0	0	1.5	400
	Total	352	93,000	117.1	30,900	96.1	25,400	565.2	149,300

overall composite wastes were highly acidic. The remaining sectors contributed predominately alkaline wastes. Specific characteristics of the wastes from the individual sectors are presented in Table V-5. The various sectors (except 3 and 5) had high BOD values ranging from 11,800 to 20,000 mg/l. Total suspended solids (not shown in Table V-5) were found to be negligible; however, some settleable solids were evident. These settleable solids when washed with distilled water are readily redissolved into solution. All wastes had high nitrogen content with Sectors 3 and 5 containing the least amounts. The phosphorous content was negligible.

Because the wastes were known to contain large amounts of various organic and inorganic chemicals, they were expected to be toxic. Consequently, toxicity studies were conducted on the flows from Sector 8, the composite flow from all sectors, and the total wastes from all sectors excluding Sector 8. The standard bioassay test was employed with the fish species, Barbus ticto, Puntius puntius and Cyprus carpio communicus. The 1970 bioassay results at the Hyderabad plant were as follows (54):

Source of Waste	48-hr TL_m (% by vol)
Sector 8, after lime neutralization to pH 7.0, followed by sand filtration	26.0
Composite flow from all sectors, after sodium hydroxide adjustment to pH 7.0	0.29
Composite waste from all sectors, excluding Sector 8, pH 9.2	0.27

With or without extensive neutralization, the wastes continued to be extremely toxic. Flows from Sector 8 were less toxic, but only after this waste stream received pH adjustment from 0.6 to 7.0.

Upjohn Laboratories, Kalamazoo, Michigan

[See Section VIII: WASTE TREATMENT AND DISPOSAL: OTHER TREATMENT METHODS.]

BIOLOGICALS

Eli Lilly Greenfield Laboratories, Greenfield, Indiana

The production of antitoxins, antisera and vaccines generates wastewaters containing animal manures, carcasses and organs, body fluid, blood, fats, egg fluids and egg shells, spent grains, biological culture

Table V-5

Composition of Wastewaters from Individual Sectors, Hyderabad, India Plant, 1970 (54)

Parameter	Sector 1 (Sulfa)	Sector 2 (Vitamin B_1)	Sector 3 (Other Vitamins)	Sector 4 (Antipyretic, Anti-TB)	Sector 5 (Sodium Metal Use)	Sector 7 (Phosgenation)	Sector 8 (Intermediates)	Total All Sectors but #8)	Total All Sectors
Flow, cm^3/day	61	26.2	17	56	41.5	0.3	307	202	509
pH	9.0	10.0	3.0	10.9	11.9	11.0	0.6	9.3	0.8
TS (percent)	11.8	0.7	5.1	9.7	3.5	5.6	8.3	7.7	8.6
TVS (percent)	3.2	0.2	0.5	2.0	0.1	1.1	6.7	1.7	5.0
	(mg/l)								
Total acidity ($CaCO_3$)	*	*	2,500	*	*	*	57,600	*	32,200
Total alkalinity ($CaCO_3$)	12,700	24,500	*	8,900	4,100	235,000	*	10,800	*
Chlorides (Cl)	22,500	4,500	4,000	8,500	14,500	8,000	20,500	17,000	18,500
Sulfates (SO_4)	25,600	1,700	14,800	14,800	2,400	4,900	37,000	14,800	28,000
Total nitrogen (N)	10,000	8,600	130	2,400	430	*	6,200	5,200	6,100
Phosphorous (P)	*	*	*	*	*	*	*	*	*
BOD	17,500	20,000	1,600	15,000	1,600	19,300	9,400	15,300	13,000
COD	31,600	33,100	3,200	27,800	3,500	43,100	13,700	28,500	19,700

* Negligible

media, feathers, solvents, antiseptic agents, herbicidal components, sanitary loads, and equipment and floor washings (6, 31). These wastes are characterized by high BOD, COD, TS, colloidal solids, toxicity, color and odor. In many instances antitoxin and antisera wastes from production and research can carry highly dangerous pathogens and specialized toxic chemicals as benzene, phenols, cresols and mercury compounds. Presence of these materials often causes serious difficulty in analyzing the wastes by standard analytical procedures. In the mid-1950's the mixed wastes from the Greenfield Laboratories amounted to 56,800 l/day (15,000 gpd) and had the following characteristics (31):

Component	Content
BOD	1,000 to 1,700 mg/l
TS	4,000 to 8,500 mg/l
TVS	3,000 to 7,500 mg/l
SS	200 to 800 mg/l
pH	7.3 to 7.6
Color	Brownish-red

By the late-1950's, the facility had grown appreciably (70). The problem was not the large wastewater volume but rather a host of scattered waste sources requiring special pretreatment measures. The wastes were categorized as:

1. animal wastes from test animals
2. pathogenic or infectious wastes from laboratory sectors conducting research on animal disease
3. toxic chemical wastes originating from laboratory sectors conducting research upon bacteriological, botanical and zoological problems
4. wastes from production of antisera and antitoxins
5. overall plant sanitary wastes.

The combined wastewaters were averaging 680 m^3/day (180,000 gpd) with the maximum flow rate approximating 1,820 m^3/day (480,000 gpd). The unit waste loads from various animals including horses, cattle, calves, pigs, rabbits, mice, monkeys, dogs, cats and pouts varied from 0.8 to 80 l/day (0.2 to 20.0 gpd) per animal and from 0.007 to 2.9 kg (0.016 to 6.50 lb) BOD/day/animal. Raw waste characteristics are given in Table V-6.

DRUG FORMULATION

Dorsey Laboratories, Lincoln, Nebraska

[See Section VIII: WASTE TREATMENT AND CONTROL: ACTIVATED SLUDGE; Drug Formulation.]

Table V-6

Raw Waste Characteristics

Eli Lilly Greenfield Laboratories, Indiana (70)

Plant Area	Flows				BOD			Total Solids			Settleable Solids	
	Ave		Max									
	(m^3/day)	(gpd)	(m^3/day)	(gpd)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	(kg/day)	(lb/day)
Antisera/antitoxins production	204	54,000	655	73,000	200-400	45-73	100-160	760-1,520	154-308	340-680	41-77	90-170
Additional anti-influenza vaccine production	250	66,720	383	101,000	40-80	9-23	20-50	100-200	27-50	60-110	4.5-14	10-30
Plant science and animal research	204	54,000	708	187,000	810-1,620	186-367	410-810	1,220-2,450	249-499	550-1,100	64-354	140-780
Monkey storage areas	18	4,700	83	22,000	800-1,600	14-27	30-60	770-1,540	136-272	300-600	136-272	300-600
Total (avg)	680	179,400	1,820	480,000	380	254	560*	860	567	1,250*	122	270*

* Maximums of 1,080 lb/day BOD, 2,690 lb/day TS, and 1,080 lb/day settleable solids

VI. WASTE PARAMETERS OF SIGNIFICANCE

Some important parameters in disposing of wastes generated from the pharmaceutical industry are given by Molof and Zaleiko, 1965 (25). Major monitoring parameters for waste streams include BOD, variation in BOD from hour to hour, toxic chemicals, color, odor, solids (dissolved, colloidal and suspended), temperature, and variation in hydraulic loading. The ammonia and organic nitrogen content in pharmaceutical wastes is of increasing concern. These loads sometimes equal or exceed BOD loads in the wastewater and cause damaging effects on fish and wildlife. Within the treatment system, key parameters include DO, COD, and turbidity.

This section focuses on studies which have dealt with *BOD*, *toxicity*, and *nitrogen reduction*.

BOD: A QUESTION OF RELIABILITY

Abbott Laboratories, North Chicago, Illinois

Nedved, Bergmann and Comens of Abbott Laboratories (75) defend the usefulness of the Biochemical Oxygen Demand (BOD) test if the nature of the analysis is appropriately interpreted and understood. The Abbott Environmental Pollution Abatement and Control Group felt that:

1. The standard BOD test, when carefully and conscientiously performed, is significantly reproducible
2. The test provides extremely valuable information in a ... variety of ways and can be applied to many ... practical problems
3. In general, there is no other single analytical parameter applied to water analysis that even approaches the information value of a standard BOD determination
4. The BOD test should not be used independently as a basic parameter, but it should be augmented with companion analyses and admittedly subjective evaluations.

The Group enumerates a number of specific uses for data derived from the BOD test, including determination of toxic and inhibitory effects of waste materials. They point out that the "logical and uncomplicated approach is to accept the BOD test for what it is -- an indirect indication of biological activity measured under somewhat controlled conditions by the uptake of oxygen in unstable, 'individualistic' biological systems."

The Abbott personnel indicate the limitations of the test must be recognized and accepted. A major disadvantage of the test is that it requires 5 days for completion. The ASTM has described additional

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limitations of the test as: a) BOD_5 cannot be considered as a quantitative expression without an approximation of the rate of oxidation and the ratio of BOD_5 to ultimate oxygen demand; b) the BOD_5 values of different industrial wastes are not (necessarily) additive; and c) the efficiency of a biological treatment process may not be accurately determined on the basis of a BOD_5 influent and effluent. Abbott states it was not the intent of its paper to deny or dilute the limitations of the BOD test, but rather to promote the advantages of the BOD analysis within the confines of the known limitations.

The BOD analytical procedure was studied in detail, including quantification of the seed used in the BOD test since pharmaceutical samples generally required seeding. The seed was obtained from the Abbott sanitary sewer, settled and gauze-filtered before use. A study was conducted on a formulated sample of acetone, sodium lauryl sulfate, sodium propionate, and water. The theoretical TOC was calculated to be 125,728 mg/l and the theoretical TOD (∿ ultimate BOD) was 444,022 mg/l, which gives a calculated TOD to TOC ratio of 3.54. When conducting BOD on replicate samples at four concentrations, the results shown in Table VI-1 were obtained.

Table VI-1

BOD_5 Determinations of Acetone Mixture (75)

Sample Level Concentration (%)	BOD (mg/l)	BOD Replicate Averages (mg/l)	Replicate Standard Deviation (mg/l)
0.003	170,327 169,640 183,820	174,595	±6,529
0.002	335,980 329,160 335,460	333,533	±3,100
0.0015	333,950 352,830 339,350	342,043	±7,940
0.001	361,260 365,300 371,380	365,980	±4,182

As the concentration of the sample increases, the BOD decreases, first gradually between the 0.001 and 0.002 percent concentrations (attributable to slight inhibitory effects), and then substantially between the 0.002 and 0.003 percent concentrations (attributable to marked inhibitory effects). This type of inhibitory behavior was commonly observed for many chemical process waste streams.

From these results, it was speculated that the BOD of an extremely dilute acetone mixture sample would be about 400,000 mg/l, compared to the calculated theoretical TOD of 444,022 mg/l. Conversely, an acetone mixture of 0.004 percent or greater concentration, would show a high level of toxicity approaching a zero BOD_5 value.

The following conclusions were drawn:

1. One of the major reasons for "perpetual misinterpretation" of the results of a BOD analysis is the futile and unnecessary search for an absolute definition of BOD. A universally acceptable definition is highly unlikely, and this very probability adds to the attractiveness and value of the test. Since the test uses a dynamic system, the response is necessarily difficult to interpret. The test also suffers from over-study and misinterpretation, which creates undue preconceptions. This test does not provide an absolute measurement, but rather (according to the authors), it should be construed "as a subtle suggestion, a reflection, of an oxygen demanding property of a sample".
2. BOD values should not be utilized independently, but TOC, TOD, and COD should be obtained to compliment BOD results.
3. A subjective evaluation of the composite information and optimistic interpretations of the BOD results are justified on the basis that, at the present time, no other procedures can adequately supplant the BOD test (75).

Dorsey Laboratories, Lincoln, Nebraska

Anderson (2,38), in 1968-69, studied the character, treatability and reduction in pollution loads passing through the Dorsey extended aeration treatment facility. Toxic constituents were thought possible in the wastes, and consequently BOD samples were seeded with specially-developed mixtures of river water and sewage, taken from the city of Lincoln and the Dorsey Labs' treatment works.

Besides conventional 5-day BOD's, samples were prepared for "continuous monitoring". Data thus obtained was used to correct for time lag and nitrification. Even with seeding, lag periods up to 2 days were encountered in certain samples. No chemicals were added to inhibit nitrification. Corrections for nitrification were necessary on a number of the BOD samples. The BOD value was found to increase with dilution, indicative of a waste containing toxic or inhibiting substances.

The authors emphasize the difficulty of obtaining reliable BOD data for industrial wastewaters, especially when inhibiting substances are present and/or the characteristics of the waste stream are highly variable.

Experiments in Great Britain

Based upon his experience in Great Britain, Lines (10) has observed that apparent BOD's obtained from using fully acclimated seed may be more than three times greater than normally determined values. This was found even for fermentation wastewaters, which are relatively biodegradable although strong.

Microbial breakdown by organisms may be impeded either by the nature of the organic materials or by antibiotic residues. If oxytetracycline, an antibiotic residue, is present in the raw wastes, a possible counter measure is treatment with ferric chloride, whereby an inactive complex is formed through the OH^- group.

TOXICITY

In the handling and disposal of pharmaceutical effluents, toxic chemical compounds are frequently encountered. Certain toxic chemical compounds are rated as extremely dangerous physiologically to humans and animals. Other compounds may seriously impair biological growths and metabolism within waste treatment systems.

Howe, 1961 (62), reported on experimental studies with potent *antibiotics*, a *phenol-mercury* substance, a selected *hormone*, and substances containing *formaldehyde and methyl alcohol*.

Antibiotics

Certain antibiotics are bactericidal whereas others are only bacteriostatic. Bactericidal refers to actual killing or splitting of bacterial cells. Bacteriostatic refers to the properties of inhibition, that is decreasing, or halting, the growth of bacterial forms. No claims are made regarding fungal or viral forms. A very small dosage of antibiotics may inhibit specific organisms, but a higher concentration is generally necessary to inhibit biological growths in an oxidation system because of the diversity of organisms present.

When the antibiotic concentration in a biological oxidation system reaches the toxic level, the biological flocs disperse or disintegrate. The microbial population may become acclimated to the antibiotic, particularly if a carefully controlled amount of the chemical is continously introduced; but then again, the system may not acclimate at all. Also, the system may acclimate to one antibiotic, but may fail when a second antibiotic is introduced. Table VI-2 presents concentrations of antibiotics known to be inhibiting to various bacterial forms.

TABLE VI-2

Minimum Concentrations of Antibiotics
Required for Complete Inhibition of Organisms[a] (62)

Affected Organisms	Penicillin (mg/l)	Streptomycin (mg/l)	Aureomycin (mg/l)	Chloramphenicol (mg/l)	Ilotycin (mg/l)
Ps. Aeruginosa	Profuse Growth	50-1,000	50-1,000	200-1,000	250
B. Proteus	10-1,200	12.5-1,000	12.5-400	3.1-50	250
Esch. Coli	38-6,000	6.3-1,000	3.1-25	3.1-25	62.5
A. Aerogenus	375-6,000	0.8-1,000	6.3-200	3.1-50	--
K. Pneumoniae	5-600	0.8-1,000	6.3-50	1.6-25	62.5

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[a] Original data from Frank, Wilcox, and Finland (1950) and from Wick, Eli Lilly & Co. (1961). The word "complete" is not defined by Howe (62). From 18 to 25 strains of bacteria utilized for each numerical entry.

Lab experiments were conducted on the effects of three antibiotics on small-scale activated sludge reactors. Total solids content in the systems was maintained at about 8,000 mg/l with acclimated sludges. Nutrients were added, the pH level was maintained at 7.4 to 7.6, the temperature was 32°C (90°F), and air was supplied. *Antibiotic A* was introduced to the system at an initial concentration of 210 mg/l, and the aeration system operated for 24 hr. Results showed that the biological system performed satisfactorily, and at the end of 24 hr, there was 93 percent BOD removal and almost 93 percent removal of the antibiotic (determined by spectrophotometric assay). Initial and final BOD values approximated 4,200 mg/l and 300 mg/l, respectively. BOD reduction was slow in the first 4 to 8 hr, after which the removal rates increased significantly.

The second antibiotic was a wide spectrum type known as *Antibiotic B*. This substance was introduced to the system at an initial concentration of 900 mg/l, and pH 7.8 was maintained. Over a 12 hr aeration period, measurements showed little or no decrease in antibiotic concentration, no removal of BOD, and not only a decrease in microbial population but also a general dispersion of the biological flocs. A second test was run using an initial concentration of 200 mg/l of *Antibiotic B* and the mixture was aerated for 24 hr at pH 7.4. In this case, the antibiotic remained stable over the first 4 hr or so but then it was reduced about 94 percent over the next 16 to 20 hr. The microbial population increased, after an initial setback during the first 8 hr. The BOD was reduced 96.7 percent from 6,200 mg/l to 200 mg/l.

Antibiotic C was a relatively powerful agent known to be stable under any pH condition. This antibiotic was added to the aeration system at an initial concentration of 400 mg/l. After 12 hr the system showed no reduction of BOD or antibiotic activity. Furthermore, the microbial population declined and was converted into dispersed forms. Fresh activated sludge previously acclimated to *Antibiotic C* in another series of experiments was added to the system. After about 8 hr, the system started to function normally, and over 24 hr of full aeration, the antibiotic was reduced 96 percent, and BOD was reduced 94.5 percent from approximately 5,500 mg/l to 300 mg/l.

The above experiments on biological oxidation of antibiotics demonstrate that biological growths can be significantly, if not totally disrupted by various antibiotics. However, remedial measures in acclimating the system and achieving recovery are also demonstrated.

Both *Antibiotics A* and *C* are described as "macrolide" antibiotics, produced by two different species of Streptomyces organisms. The chemical features of this class of antibiotics are a large lactone ring, a ketone function, and an amino-sugar attached by glycosidic linkage. *Antibiotic A* contains a phenoxymethyl group. Biological degradation is thought to proceed by oxidation and hydrolysis of the antibiotic. When excessive amounts of these macrolide antibiotics are present in the aeration system, the antibiotics and their degradation derivatives are both toxic to certain micro-organisms. Some organisms may be able to acclimate to the antibiotic(s), lowering antibiotic concentration, whereby levels are favorable for continuous functioning of the biological treatment system. Unfortunately, no data was obtained relative to full-scale systems and their adaptability and/or vulnerability to the dynamic situation in an ongoing pharmaceutical manufacturing installation.

Phenol-Mercury Compound

The particular phenol-mercury studied was a highly bactericidal compound of sodium ethylmercury thiosalicylate (Thimerosal, Lilly) and sodium o-phenylphenate (Lilly). This compound is used both for disinfection and sterilization. A wastewater containing this compound received treatment. This waste was found to contain 6.9 mg/l mercury, 286 mg/l total phenylphenate, 15,000 mg/l emulsified oil, 83,400 mg/l total solids, and 160,000 mg/l BOD with a pH of 7.9.

The experimental treatment consisted of two alternate systems. *Primary Treatment A* involved breaking the oily emulsion of the phenol-mercury waste by sulfuric acid treatment at pH 1.5. *Primary Treatment B* consisted of acid cracking, plus lime-aluminum coagulation together with bentonite and sludge additions to aid coagulation, followed by settling. These two effluents were then aerated 8 hr employing acclimated, activated sludge. The results of the two treatment systems are shown in Table VI-3.

After chemical treatment and settling, the phenol-mercury waste was successfully treated by activated sludge with about 99.9 percent reduction of phenylphenate, and the mercury concentration decreased from 6.9 mg/l to 0.05 mg/l. However, data are lacking on the conventional parameters to sufficiently assess the biological oxidation capabilities of these systems. In the biological degradation of the phenol-mercury compound, breakdown of the sodium ethylmercury thiosalicylate is thought to result from oxidation and/or reduction cleavage of the compound with attendant release of mercury from the organic structure. The mercury can be oxidized to HgO and/or Hg_2O_3. Sunlight is also believed responsible for dissociation of mercury. The sodium thiosalicylate and the ethyl components are subsequently broken down into the intermediates such as benzoic acid, succinic acid, acetic acid, etc., and eventually into the simple end products.

Table VI-4 gives the results of additional experiments in which varying concentrations of raw waste and *Primary Treatment A* and *B* effluents were fed into the activated sludge process and aerated for 8 hr. The activated sludge process could tolerate but not successfully treat the given concentrations of raw emulsified waste.

Hormone

The next phase of investigations involved the experimental degradation of the female sex hormone, DES, by aerobic and anaerobic treatment.

TABLE VI-3

Effluent Quality From Experimental Treatment Systems Receiving Phenol-Mercury Wastes (62)[a]

Parameter	Emulsified Raw Waste	Primary Treatment *A*	Primary Treatment *B*	Primary Treatment *A* + Activated Sludge	Primary Treatment *B* + Activated Sludge
pH	7.9	1.5	6.7	7.4	7.3
TS	83,400	26,900	7,740	1,600	1,350
TDS	8,600	21,000	5,000	1,320	1,210
Total Hg	6.9	0.85	0.02	0.05	0.05
Total Phenyl-Phenol ($C_6H_5C_6H_4OH$)	286	14.0	23.7	<0.005	<0.005
TL_m, 48 hr (% conc.)	0.3	0.5	12.0	b/	b/

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a/ Data given in mg/l, except pH and TL_m.
b/ No toxicity recorded.

TABLE VI-4

Activated Sludge Treatment of
Raw and Chemically Pre-treated Phenol-mercury Effluent (62)

Waste Concentration	Emulsified Raw Waste (mg/l)			Primary Treatment *A* (mg/l)			Primary Treatment *B* (mg/l)		
	1%	2%	5%	1%	2%	5%	1%	2%	5%
Initial BOD	2,800	5,700	9,100	400	700	1,620	250	590	1,100
Final BOD	1,700	3,700	8,100	210	450	820	110	270	550
Toxic to test fish	--	Yes	--	--	No[a]	--	--	No[a]	--

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[a] At 40% concentration, both A and B were toxic to fish. Unfortunately, methodology not explained in arriving at toxicity observations.

DES in very low concentrations is highly bactericidal. The limit for instantaneous contact with DES is 0.22 g/kg (0.1 g/lb) of carrier material and, therefore, extreme care was taken in handling this waste. A 3.8 liter (1 gal) chamber was used for the activated sludge studies and a 3.8 liter container for the digestion experiments. DES was mixed into a carrier and this waste mixture was placed into the aerator in the ratio of 1 volume waste to 6 volumes activated sludge. Activated sludge treatment was conducted for 14 continuous days, the results of which are shown in Table VI-5.

Treatment required an unusually long time, although the DES reduction was 94 percent after 7 days and 99 percent over 14 days. When the initial concentration of DES in the feed to the aerator was lowered from 204 mg/l down to 5 mg/l, reduction of DES over 24 hours of aeration was measurably improved. However, even at these low concentrations, some inhibition of activated sludge growths was evident. The experimental data suggested that perhaps the strong DES wastes could be treated in a long-term aerated lagoon, and the diluted waste could be treated by activated sludge. However, neither approach appeared feasible because hygiene practices and safety precautions associated with handling of DES from the batch production program were considered too strict and time-consuming.

In the anaerobic digestion experiment, the DES waste was added to the digestion chamber in the ratio of 1 volume waste to 2 volumes digested sludge. Temperature was maintained at approximately 32°C (90°F) and digestion was conducted for 14 days. After 7 days of digestion, BOD and DES removals were respectively 83.9 and 86.0 percent. After 14 days, BOD reduction was 94.6 percent and DES reduction was 99.0 percent. These results were comparable to those obtained by activated sludge treatment of the strong DES waste for 14 days.

Formaldehyde and Methyl Alcohol

Howe (62) also conducted limited evaluation studies on the treatability of formaldehyde and methyl alcohol wastes by activated sludge. Activated sludge and the waste material were added to a 3.8 liter (1 gal) aeration chamber with the MLSS maintained at 6,000 mg/l. In separate experiments, the initial methyl alcohol and formaldehyde concentrations in the aerators were 1.05 and 0.25 percent, respectively, and aeration was conducted for maximum periods of 6 hr. Methyl alcohol was analyzed by the refractometer from the distillate of each sample. Formaldehyde was determined by the spectrophotometer. The methyl alcohol level was reduced 81 percent after 2 hr, and the formaldehyde was reduced 87 percent after 4 hr. The organics may have been partly removed via volatilization during aeration. No toxicity effects were observed in these test runs.

The biochemical decomposition of formaldehyde may proceed two ways. The formaldehyde may combine with protein molecules in the sludge and be removed by clarification, or the formaldehyde may be oxidized into

TABLE VI-5

Activated Sludge Treatment of Hormone (DES) Wastes (62)

		204 mg/1 DES Waste; 14 Days Aeration					
Aeration Period	pH	TS (mg/1)	TDS (mg/1)	DES (mg/1)	DES Reduction (%)	BOD (mg/1)	BOD Reduction (%)
0 days	7.6	50,000	45,000	204	--	28,000	--
7 days	8.4	27,900	10,800	10	94.0	3,000	89.3
14 days	8.5	13,200	5,900	2	99.0	1,000	96.4

		5 mg/1 DES Waste; 24 hr Aeration					
Run Number	pH	Initial DES (mg/1)	Final DES (mg/1)	DES Reduction (%)	Initial BOD (mg/1)	Final BOD (mg/1)	BOD Reduction (%)
1	8.2	5	1.7	66.6	18,100	3,100	82.9
2	8.4	4	1.2	70.0	17,000	2,800	83.5
3	8.5	3	0.8	73.6	15,800	2,400	84.8
4	8.6	1	<0.2	>80.0	14,600	2,100	85.6

formic acid and methanol as the intermediates, which in turn break down into carbon dioxide and water. The biochemical decomposition of methyl alcohol is thought to be somewhat similar to that for formaldehyde.

NITROGEN REDUCTION

NPDES discharge permits for bulk pharmaceutical manufacturing installations are focusing on necessary and substantial reduction of ammonia and organic nitrogen in the associated wastewaters. Waste streams from these installations, even after reasonably high levels of biological treatment, may still contain from a few hundred to a few thousand mg/l of Kjeldahl nitrogen. Ammonia and organic nitrogen loads may substantially exceed BOD loads in the final discharges and range from 454 kg (1,000 lb)/day up to 3,630 kg (8,000 lb)/day.

Impacts due to nitrogen compounds include: the oxygen demand of nitrogen compounds; ammonia toxicity to fish and wildlife; increased chlorine demand due to ammonia and related compounds; formation of chloramines and similar constituents during chlorination which are decidedly toxic to fishlife; off-tastes to water supplies; and health problems to humans and animals.

Also, with pharmaceutical wastes, even moderate levels of unoxidized nitrogen can give varying and possibly distorted results in running the BOD test. Regulatory authorities are now initiating standards for nitrogenous waste materials in streams and effluents. Treatment facilities will increasingly be required to produce effluents low in both unoxidized nitrogen and total nitrogen.

Loehr (117) summarizes available management methods in reducing the nitrogen content of wastewaters as shown below. Other important references include Adams (118) and Ehreth and Barth (120).

Treatment	Nitrogen Compounds Removed
Physical and Chemical	
Land Application	NH_3, NH_4+, organic N
Electrochemical	NH_4+
Ammonia stripping	NH_3
Ion Exchange	NO_3-, NH_4+
Electrodialysis	NO_3-, NH_4+
Reverse osmosis	NO_3-, NH_4+
Breakpoint chlorination	NH_4+, organic N
Biological	
Nitrification	NH_4+ (NH_3) conversion to NO_2- and NO_3-
Algal utilization	All forms
Microbial denitrification	NO_3-, NO_2-
Land application	All forms

VII. WASTE RECOVERY AND CONTROL

In general, wasteloads from pharmaceutical manufacturing operations can be reduced either by recovery of valuable solvents, or by recovery of certain components in the form of animal feed. Both types of in-plant control measures reduce the raw wasteload to treatment facilities. Examples of each type of control are given below.

SOLVENT RECOVERY

Solvent pretreatment has a twofold objective: to recover solvents, and to favorably impact the waste disposal problem. This pretreatment lowers the BOD and reduces toxicity of the spent liquors. As a result of the heat of distillation, the character of these wastes can be modified by the formation of solids and tarry compounds. Ultimate disposal of the most deleterious wastes is simplified by concentrating them in as small a waste volume as possible. Weaker wastewater from other sources in the plant can then be treated or disposed of by more conventional methods (13, 59).

The impact of solvent wastes on waste treatment facilities is significant because of the high BOD levels. As an example, a commercially used ketone solvent has been reported (25) to yield a BOD level of 2,000,000 mg/l, about 9,000 times stronger than normal untreated domestic sewage. A gallon of this solvent is equivalent to raw domestic wastes from a city of 77,000 people. A second solvent, amyl acetate, was reported to have an approximate BOD of 1,000,000 mg/l (32,65). Thus, a small variation in solvents lost to waste streams has a great impact upon a treatment plant and/or receiving watercourse.

Among the methods used in recovery are single- or multi-effect distillation units. In other cases, solvents may be incinerated. Molecular sieves have also been used in purifying spent organic solvents (6).

Solvent recovery not only represents savings in cost of raw materials to the production department but also means considerable savings in waste disposal costs. Automated monitoring has been recommended on all effluent lines especially for developing a material balance analysis. Monitoring is particularly important on waste streams originating from the solvent recovery areas. The monitors can be wired into an alarm system to immediately detect and warn of malfunctioning processes, surges, spills, or other accidental discharges (25).

At Bristol Laboratories, Syracuse, N.Y. in the early 1950's, solvents were recovered by two methods (65). Solvents and fermentation broth were passed downward through a 1.8 m diam. by 9.1 m high (6 by 30 ft) stripping column. The broth percolates down and around a series of plates and bubbler caps. Live steam enters the bottom of the column. Distillates off the top of the columns are condensed for solvent recovery and spent broth leaves the column at the bottom. The second system for solvent recovery at Bristol Laboratories is a combined stripping and rectifying column from which it was possible to remove all but 0.25 percent of the water from the spent solvents.

BYPRODUCT RECOVERY - ANTIBIOTICS PRODUCTION

Feasibility studies have been made for recovering spent fermentation broths and mycelia from antibiotic production (10). At least some of these products have been shown to contain unidentified growth factors for animal feeding. Recovery is accomplished by filtration, evaporation, and drying; the processed material is then sold as animal feed. While use may be limited in certain cases because of undesirable trace amounts of antibiotics, this material has been shown to be a rich source of vitamins, especially B_2 and B_{12}. A typical analysis of dried penicillum mycelium is given below (10).

Content	Percent	Content	μg/g
Moisture	8	Aneurin	6
Crude Protein	32	Niacin	7
Fat	7	Pantothenic acid	64
Fiber	7	Riboflavin	37
Ash	20	Choline	3,700
Carbohydrate	26	Pyridoxin	13
		Biotin	5

A typical scheme developed for recovery of antibiotics production wastes is that based on a feasibility study conducted for a waste recovery system to be installed on a new antibiotics plant operated by Abbott Laboratories in Barceloneta, Puerto Rico (22). According to this scheme, fermentation beers would be segregated and solvents and antibiotics stripped. It was believed that virtually all the mycelium, solvents and antibiotics could be recovered. After a thorough study of alternate treatment and disposal methods, the company decided to completely segregate the spent fermentation beers. Subsequently, this bulk material would be concentrated by triple-effect evaporators to 30 percent solids, or higher (a method similar to that used at Abbott's North Chicago, Ill. facility).

Immediate plans called for handling this concentrated material onsite in an odor free, refractory incinerator with the exhaust air discharging into the main boiler stack. Future provisions called for adding suitable drying equipment when a local market could be developed for the fermentation solids. The company stated that concentration and incineration would provide for complete destruction of the BOD and solids in the spent beer streams, and that no conventional secondary treatment operation could equal this degree of treatment. Although Abbott's development plans for Barceloneta did not envision complete treatment for the overall antibiotics complex, zero waste discharge was indicated as being economically feasible for the fermentation processing areas. More recent information, however, creates some doubt as to whether this proposed waste recovery was accomplished.

As early as 1952, Edmondson (60) described the large-scale recovery and disposal of penicillin and other antibiotic spent beers by triple-effect evaporators at Upjohn Company's Kalamazoo, Mich. plant. In 1951, when Upjohn expanded its fermentation production facilities, BOD loads entering the existing trickling filter waste treatment plant rose from 1,530 to 3,600 kg (3,500 to 8,000 lb)/day. Various antibiotics were generated from deep vat fermentation, and at least four major types of antibiotic spent beers were handled. Most of the residual extraction solvents were removed by azeotropic distillation before evaporation. Certain broths were quite low in pH and were consequently neutralized with 50 percent caustic before evaporation. The spent beers were stored to equalize loads onto the evaporator. Excess beers not capable of being handled in the evaporator system were sent to existing biological treatment. Certain of the antibiotic spent beers contained substances reported as toxic to the biological system, and therefore evaporation was intended to partially minimize impact on the biological treatment works.

The spent beers from the equalizing tank with a solids content between 2.5 to 3.5 percent were received into the triple-effect evaporator at the rate of 9.5 to 11 kl (2,500 to 3,000 gal/hr.) Barometric condenser water from the third or last effect of the evaporator could be recycled as cooling water. The condensates from the first effect were sent to the boiler house. Condensates from the second and third effects, possibly contaminated from entrainment or carryover, were generally discharged to an aeration tank and then to the trickling filter plant. The multiple effect evaporator system for handling spent beers at the Kalamazoo plant was put on-line Dec. 9, 1952. The solids concentration leaving the evaporators, found to be a function of the type of beers entering the system, varied from 15 to 35 percent.

The BOD reductions directly associated with the triple-effect evaporation system were 96 to 98 percent for the four types of antibiotic spent beers. Residual BOD in the condensate streams varied from 90 to 450 mg/l. This organic BOD was substantially attributed to solvent carryover in the condensate streams. For example, Antibiotic A, which was not stripped prior to evaporation, showed the highest BOD of 450 mg/l and the least BOD reduction of 96 percent. Initiation of solvent recovery and improvement of evaporation procedures would help reduce the residual BOD. Total solids in the condensates were relatively low (75 to 150 mg/l). There was concern that the carryovers could contain some trace antibiotic activity, thereby depressing biological growths on the subsequent trickling filters. "Checks" for antibiotic activity, run both on the condensates and the concentrates, showed that practically all of this activity was carried down in the concentrates (60).

A cost analysis was made of initial capital investment, plus the annual operating costs of the evaporator system vs conventional biological treatment in handling the antibiotic beers. In this case, no credit was given for potential profit return on a saleable byproduct. Biological treatment was characterized by a much higher initial cost and lower operation and maintenance cost compared to the evaporator system. By decreasing the initial investment with the evaporator system, the standby cost is reduced, and the operating cost varies somewhat more proportionately with the volume of beer production. This situation would seem to provide the high degree of production flexibility generally required in pharmaceutical manufacturing plants. With a lower initial cost for the evaporator, the capital cost savings could be invested in a secondary profit-deriving process, producing an annual profit.

Edmondson (60) in 1953 indicated it should be possible to find a market for this concentrate material, thereby reducing annual cost of the evaporator system. The concentrate, found to be a rich source of protein and vitamins, was thought suitable for animal feed either as a dry product or a syrup. Annual cost of the evaporator system was about $0.01/gal spent beer if operated only one shift per day, but decreased to $0.0058/gal if operated over three shifts. Annual cost was otherwise estimated as $0.06/lb BOD removed.

BYPRODUCT RECOVERY - TECHNOLOGY TRANSFER FROM RELATED INDUSTRY

United States

Blaine and Van Lanen (42) describe techniques developed by the distilling and brewing industries in the 1950's and early 1960's for achieving practical waste abatement. These techniques, they felt, may be adaptable also to the newer branches of the fermentation industry, including pharmaceuticals. The "entire plant" approach has been used successfully by the distilling industry in attaining desired objectives. First, an inventory of waste sources is made, which when totalled approximates the findings of waste loads in the combined plant effluents. Such an inventory provides assessment of the relative costs of various waste abatement alternatives, including in-plant controls. It also demonstrates the cost or profit involved in major production rearrangements, such as changing types and amounts of primary products and byproducts that can be generated from a given quantity of raw materials. When BOD, COD and other analyses are diligently applied to each process unit, an accounting of waste is also an accounting of product loss.

At a Hiram Walker distillery, substantial waste abatement has been made entirely within plant, without the use of so-called conventional treatment. Wasteloads were reduced from 5.6 PE BOD/bu of grain processed in 1951-52 to 2.8 PE BOD/bu grain in 1959-60, and this was expected to drop to about 1.2 to 2.0 PE BOD/bu in the early 1960's. A 56 lb bushel is the commonly accepted unit of production in the distilling industry.

The basic processes used by Hiram Walker are described as follows. Grains are received, milled, slurried, then pressure-cooked in eight 49 kl (13,000 gal) cookers. The mash is cooled in the cookers by vacuum blowdown, saccharified with malt, and further cooled in a five-effect vacuum cooler. After yeast is added, the mash is sent to a battery of twenty-four 380 kl (100,000 gal) fermenters for 55 to 90 hr. The fermentation beer, containing the spent grain slurry and about 7 percent alcohol, is pumped to the stills. After distillation, the spent fermentation beers are sent to the feed recovery plant. This whole stillage contains about 25,000 mg/l BOD, 8.3 lb BOD/bu (∿ 50 PE BOD/bu), 5 to 7 percent solids (17 to 19 lb/bu), and a unit volume of 40 gal/bu grain (42).

The whole stillage is screened, then the screenings are pressed and dried in rotary driers. Seven rotary indirect steam tube driers provide a total finished product capacity of 10 to 12 tons/hr of dried light grains. Press liquors are returned to the feed recovery process.

The thin stillage passing through the screens is centrifuged in twelve basket centrifuges. Then it is evaporated using two parallel sets of triple-effect evaporators and finishing pans. Evaporated syrup, at about 35 percent solids, may be dried directly on drum driers to produce *distillers solubles*. Otherwise, it is mixed with the screened grains and sent to rotary driers to give a product called *distillers dried grains with solubles*. The following table summarizes the Hiram Walker in-plant waste survey, completed in 1953.

Process Area	PE BOD/1,000 bu mashed	(%)
Cooking and fermenting, incl. cleanups	371	12.3
Distillation	55	1.8
Feed recovery plant	2,510	83.4
Powerhouse	73	2.4
Total	3,009 = 3 PE/bu	100.0

In 1954, of the 2,510 PE produced from the feed recovery plant, 945 PE were eliminated by completely recovering and converting into feeds the solids from the drum dryer vapor scrubber and from the dust collector on the dried grains dryers. The remaining 1,565 PE were attributable mainly to condensates from the triple-effect evaporators. The company stated these wasteloads can be reduced at least 50 percent if the existing equipment is operated under tightly controlled flow and temperature conditions. Residual PE from the feed recovery plant is now estimated at 750 PE, or less. The residual with these changes is estimated as about 1.25 PE BOD/bu grains processed (42).

Without feed recovery, waste materials represent 50 to 55 PE BOD/bu. Recovery of screenings reduces the wasteload to 40 to 45 PE, whereas drying of total stillage leaves less than 2 PE BOD/bu, or a 96 to 97 percent waste reduction accomplished by good in-plant control and recovery procedures. Blaine and Van Lanen describe various feed recovery operations as having produced net profit and in most cases generating enough revenue to have paid for capital equipment costs. Annual market value of feed byproducts from the entire U.S. grain distilling industry as far back as the 1950's was estimated at $20 million annually, which undoubtedly has increased greatly through the present (42).

England

Based on experiences in Great Britain, Jackson (48) compares the various fermentation industries and examines the status of each. The fermentation industries are those in which micro-organisms such as yeasts, molds and bacteria are either used under closely controlled conditions to produce desirable end products, or are incorporated into processes where their presence contributes significantly. Apart from the brewing, wine and distilling industries, Jackson defines other activities as including the production of antibiotics, bakers' yeast, organic acids, solvents, cheese, silage, and processes such as the retting of flax. The effluents from the distillation of whiskey contain about one-third of the organic matter originally used in fermentation, whereas for antibiotics the proportion is much higher. Breweries and wineries are in a more fortunate position, since most of the raw materials used in these industries eventually end up in the bottle or cask with less potential wasteloads in the final effluents. From many of the fermentation processes, the micro-organisms are simply released into the effluents, and one example is cited of yeasts being freely wasted from the production of alcohol.

From malt and grain whiskey production, waste is reduced significantly by recovering the solids which otherwise would be present in the effluents. The husk and coarse insoluble matter from the mashing stage is sold as "wet grains," at about 80 percent moisture content, or subsequently dried for lower transportation costs. Additional solids can be recovered from grain-spent washes by filtering through fine screens followed by evaporation of the liquors.

Solids recovery produces greater economic return when the operations are relatively large and the price for dried materials approximates or exceeds production cost. The solids in malt spent wash are nearly twice those in grain spent washes, which indicates greater potential revenue return for malt whiskey distilleries. However, Jackson mentions that malt distilleries are considerably smaller than grain distilleries. Evaporation of malt whiskey spent wash in Scotland has been determined as economical only if a central evaporation plant serving many distilleries is fed a minimum of 1,500 kl (400,000 gal) of spent wash per week. Most grain distilleries are large enough to give an economical return on evaporation.

Since 1966, the economics of spent grains recovery have generally become much more favorable. Byproduct conversion of only these waste streams does not, however, represent an adequate solution in many cases. Other wastes, including the evaporation condensates, steep water, spent lees, and miscellaneous washes must also be treated, converted to suitable byproducts, or otherwise safely disposed of. The subject byproducts are a good source of protein and contain appreciable amino acids, B vitamins, and unidentified growth factors for compounding into desirable animal feedstuffs (48).

In the production of antibiotics and vitamins by fermentation, yields of the desired values are quite small and therefore the potential wastes are nearly equal to the quantity and strength of the incoming raw materials. Jackson (48) states if the bacterial cells or fungal mycelium are not contaminated with filter aids, it is possible to recover and use this mycelium for animal feeding either in the wet or dry form. Penicillin wastes have been found to contain valuable growth factors. Mycelium and likewise evaporated and spray-dried solubles from penicillin, riboflavin, streptomycin and vitamin B_{12} fermentations have been used for animal feeds or supplements.

WASTEWATER REDUCTION AND RECOVERY METHODS

Bristol Laboratories, Syracuse, New York

The Bristol Laboratories plant pretreats its fermentation waste before disposal to the municipal treatment works. After studying the plant and the municipality receiving the wastes, the following measures were recommended to the industry in 1951 (32):

- Remove formaldehyde from the industrial wastes to eliminate bacterial inhibition within the digesters.
- Install stripping towers for removal of solvents.
- Remove all mycelium.
- Eliminate sources of possible leakage of process materials.
- Conduct a program of sampling and testing solvents in wastewater flows.
- Carefully program the dumping of contaminated or spoiled fermentation batches.
- Neutralize acid fermentation wastes to protect sewers and preclude interference with biological units at municipal treatment plant.
- Provide waste stream equalization.
- The manufacturer informs the proper authorities of changes in process operations so that careful consideration could be given to effects upon the municipal treatment facilities.

Bristol Laboratories incorporated many of these measures and reduced the wastewater volume by installing a recirculating cooling water system. This reduced the need for new water in this circuit from 7,570 m^3/day (2.0 mgd) to 150 m^3/day (40,000 gpd). Water consumption was reduced in the following areas:

Location	Volume Reduction	
	(l/min)	(gpm)
Air conditioning condensers	189	50
Vacuum pump cooling	76	20
Nash pumps	95	25
Vacuum ejectors	246	65
Bleed steam condensation	757	200
Total Reduction	1,360	360

Water reduction on the air conditioning units was the result of converting to tower water for condensing, and also routinely cleaning the (fouled) heat transfer surfaces in the evaporative coolers. Pumps and ejectors were converted to tower water for cooling and condensing. The volume of steam bleed condensation waters was reduced by installing control valves on the condensing water headers leading to the various bleeds required in sterilization.

Upjohn Laboratories, Kalamazoo, Michigan

[See Section VIII: WASTE TREATMENT AND DISPOSAL: OTHER TREATMENT METHODS.].

VIII. WASTE TREATMENT AND DISPOSAL

During the 1950's, there was substantial increase in the manufacture of fermentation product pharmaceuticals such as vitamins, steroids and sex hormones, and antibiotics. These products created complex waste treatment problems for the industrial facilities and the municipal treatment works which accept these pharmaceutical wastes.

Pharmaceutical plants generally combine the fermentation process with the production of synthesized organic chemicals and/or biologicals. The combinations result in a complex mixture of wastes, presenting unusual and difficult problems. The waste flows often have extremely high BOD and COD and contain toxic chemicals detrimental to biological treatment. And, depending on production scheduling and whether processing is batch or continuous, the wastes can vary widely both in strength and quantity.

The treatment of wastewaters from antibiotic production as of 1961 was thought to almost exclusively encompass biological methods, a situation that has not changed radically in the 1970's. Kempe (37) states that both activated sludge and trickling filters have been successfully employed on fermentation waste. Activated sludge is more vulnerable to shock loads, but it is less of a problem where fermentation specialists are available for good treatment plant operation. Nevertheless, severe impact on activated sludge plants is due to widely fluctuating loads and the likely presence of antibiotics and toxic solvents. These problems appear less troublesome in trickling filter installations.

Aside from *activated sludge* and *trickling filtration, other treatment methods*, such as anaerobic filters, spray irrigation, oxidation ponds, and deep well injection have been employed by the pharmaceutical industry.

Kempe concluded that the wide diversity, in itself, of treatment processes used for pharmaceutical wastes attests to the fact that all the answers to these waste problems are not yet available.

ACTIVATED SLUDGE

Fermentation

Design Criteria for Pharmaceutical Wastes

Eckenfelder and Barnhart (27) give design considerations and criteria in activated sludge treatment of pharmaceutical wastes, particularly those originating from fermentation activities. For wastes containing spent broths, nitrogen and phosphorous are usually present in sufficient quantities for biological oxidation, but this may not always be the case.

BOD loads to an activated sludge treatment system are most frequently reported in terms of lbs daily BOD/1,000 ft^3 aeration basin or lbs daily BOD/lb MLVSS. At high concentrations of BOD in the aeration basin, the rate of removal of BOD will be roughly proportional to the concentration of viable activated sludge present (MLVSS). However, at relatively low concentrations of BOD in the basin, the rate of removal of BOD progressively decreases and is more or less proportional to the remaining concentration of BOD. Significant differences are expected between batch treatment vs a continuous, completely mixed treatment process. In batch treatment, the BOD removal rate will be more or less constant and proportional to the MLVSS level until a limiting BOD concentration is reached. Below this point, the rate of BOD removal will decrease and be proportional to the concentration of BOD remaining at any time. In a continuous system, the BOD concentration of the aeration basin is equal to that leaving the tank, and the rate of BOD removal will be dictated by the effluent BOD concentration. Rates of BOD removal must be determined experimentally for each pharmaceutical waste by developing data from laboratory bench studies or pilot-scale plants.

In selecting aeration equipment for the activated sludge basin, the oxygen requirements of the micro-organisms and the transfer characteristics of the oxygen into the wastes must be known. At high BOD loading levels, oxygen utilization rates as high as 120 mg O_2/hr/g VSS have been observed. When BOD removals are nearly complete, the utilization rate decreases to very low levels (5 to 10 mg O_2/hr/g VSS). Total oxygen requirements are related to the BOD removed and the MLVSS concentrations by the following expression which is determined experimentally in the lab or by pilot-plant setup:

$$\text{kg (lb) } O_2\text{/day} = a \times \text{kg (lb) BOD removed/day} + b \times \text{kg (lb) MLVSS.}$$

High-speed turbine systems for transferring high rates of oxygen into very strong BOD wastes have been used successfully by the pharmaceutical industry.

The excess or net sludge resulting from activated sludge treatment may be determined from the expression:

$$\text{kg (lb) VSS/day} = a \times \text{kg (lb) BOD removed/day} - b \times \text{kg (lb) MLVSS}$$

where "b" relates to the amount of sludge consumed through auto-oxidation.

Following the aeration process, the biological sludges can be separated from the aeration liquor by either settling or flotation. At low BOD loadings into the aeration process, settling may be successfully employed, but at high loadings, the sludges leaving the aeration basin are oftentimes highly active and will frequently gasify and float without benefit of oxygen. In this case, pharmaceutical plants have utilized dissolved air flotation for solid-liquid separation, particularly those plants dealing with spent fermentation beers.

The various processes employed for sludge disposal are thickening by settling or flotation, aerobic oxidation, anaerobic digestion, centrifugation, air drying, vacuum filtration, evaporation and recovery, burning, spreading onto land, landfilling or burial. Aerobic oxidation of sludges has been used successfully by pharmaceutical companies. However, 20 to 50 percent of the sludge is usually reported as resistant to oxidation which becomes treatment process residue.

Synthesized Organic Chemicals

Biological Treatment of Pharmaceutical Chemical Waste

Chemical manufacturing wastes can usually be treated biologically to acceptable standards economically, but extensive study is necessary to give satisfactory results (47). If within a complex effluent there are significant amounts of refractory materials, it is best to separately treat these streams by other means than to overload the activated sludge system. Wastes containing phenolics, aldehydes, organic acids and similar constituents can generally be treated economically with up to 99 percent BOD reductions.

A high level of organic removal from chemical wastes using activated sludge treatment is usually achieved only in the lower loading range of less than 0.5 kg (lb) of BOD applied per kg (lb) of activated sludge dry solids. At loadings of 1.0 kg (lb) BOD per kg (lb) solids, reductions will often decrease to less than 50 percent. With more difficult-to-treat chemical wastes, the choice must be made between single stage vs two-stage aeration. Two-stage aeration is considered by most to represent two or more separate aeration tanks in series, but strictly speaking, a system is two-stage only when it involves intermediate settling.

A chemical plant where the pollution loads comprise 70 percent citric acid process wastes and 30 percent other pharmaceutical wastes had a BOD of 1,800 mg/l. This wastewater was treated to yield a final discharge of less than 50 mg/l BOD in a single-stage activated sludge system with a loading of 4.3 kg BOD/m^3 (270 lb/1,000 ft^3)/day.

A study was made of a chemical plant manufacturing a wide array of pharmaceutical products, dyestuffs and intermediate products. Some of the contaminants were readily degraded but the remainder proved a difficult problem for the activated sludge process. With single-stage treatment it was possible only to reduce the influent BOD of 1,000 mg/l to 200 mg/l, even with 48 hr aeration. It was subsequently shown by utilizing a two-stage system with 6 hr aeration in the first stage, intermediate settling, and 12 hr of aeration in the second stage, that a final effluent of less than 50 mg/l BOD could be expected.

The oxygen demand of chemical wastes in biological treatment will generally vary between 1.1 and 2.2 kg (lb) oxygen/kg (lb) BOD removed. Oxygen demand for pharmaceutical wastes is thought to be in the range of 1.1 to 1.3 kg (lb) oxygen/kg (lb) BOD. Excess biological sludges produced from chemical wastes will usually approximate 0.2 to 0.5 kg (lb) sludge/kg (lb) BOD removed. If the sludges are thickened followed by chemical conditioning, the mixture can be passed through a rotary vacuum filter producing a cake having up to 25 to 30 percent solids. Since land disposal of these and other sludges is becoming increasingly difficult, incineration is being viewed in a much more favorable manner.

Burgess reports that the multiple-hearth furnace can provide complete incineration of the organic matter in the sludges, the end products comprising sterile ash and clean flue gases. Scrubbers, precipitators or other pollution control devices may be necessary on the exhaust air streams. Collected ash may possibly be reused as a filter aid conserving chemical costs. Although sludge incineration requires fairly large capital and operational costs, in some cases supplemental fuel or heat may not even be necessary. It is essential in every case to obtain maximum dewatering of sludges prior to incineration and to select a furnace with high heat economy. The multiple-hearth furnace is said to be well-proven and reliable for the incineration of sludges and also claimed to have the highest thermal efficiency of the various types of incinerators commercially available (47).

Nitroaniline Isomers: Biodegradation and Treatment Capability

Extremely long-term biodegradation tests were conducted on the isomers of nitroaniline, which were being used as raw materials in the manufacturing of bulk pharmaceuticals and special chemical products at an organics plant in the midwest (5, 119). The subject isomers consisted of the ortho-, meta-, and para- forms of nitroaniline used in the organic synthesis of various sulfanilamides. These sulfanilamides included formulated organic dyestuffs and a special coccidiostat used in treating poultry diseases. Of the three isomers, the company reported greatest use of the para form; the ortho was used only to a limited extent; and the meta form was eventually discontinued in production. The nitroanilines were studied because difficulties developed during treatability tests being conducted on the company's wastewaters. Although these industrial wastes were being sent to municipal facilities, the company investigated the feasibility of pretreatment and separate treatment schemes.

The first bench-scale and pilot-scale biological treatment units showed poor organic carbon removals. A persistent yellow-orange color indicated that the problems were due to the nitroanilines which were known to have toxic properties. Subsequently, long-term biodegradability studies were run on these compounds. The findings indicated that process modifications would not offer a satisfactory solution and that almost complete recovery of these materials was necessary (5, 119).

Certain organic industrial wastes are exceedingly difficult to treat biologically because they are either toxic, virtually nonbiodegradable, or only slowly oxidized so that they are not removed during the normal course of biological treatment. The company conducted biodegradability tests for 180 days to specifically determine the treatability potential of the wastes involved.

Although previous work on the biodegradation of nitroaniline was quite limited, some related investigations had been carried out on nitrobenzene, aniline, nitrophenols and nitro-benzoic acid. These results showed a wide degree of susceptibility to breakdown. The literature also indicated the possibility of cross-adaption or cometabolism, i.e. when a culture of micro-organisms has adapted to one chemical or isomer, it shows a definite tendency to degrade a related chemical or isomer. For purposes of the long-term biodegradation studies, the isomers of nitroaniline were mixed with sewage, an electrolytic respirometer measured oxygen uptake rates, and nitrification was suppressed by means of the chemical inhibitor, 2-chloro-6-(trichloromethyl) pyridine. The biochemical oxygen demand of the sewage substrate and the added nitroaniline could be separately accounted for in the oxygen utilization-time rate curves that were developed.

The first tests essentially indicated over a period of 60 days that both ortho- and meta-nitroaniline were virtually nondegradable. The para-nitroaniline, although showing no susceptibility to breakdown for the initial 20 days, exhibited significant oxygen uptake thereafter. It was indicated that all three isomers at the concentrations used in the tests were not toxic to the micro-organisms in the sewage seed. Cross-seeding was attempted with micro-organisms previously adapted to p-nitroaniline applied to new samples of meta- and ortho-nitroaniline. The results of these tests were only partially successful. Essentially, about 25 percent of the meta-isomer was degraded over a period of 50 days. There was virtually no biodegradation of the ortho-isomer.

Testing was continued, adding relatively high levels of p-nitroaniline to previously acclimated seed to determine if these high concentrations could be sufficiently oxidized and if toxic effects would occur. Initially, 50 mg/l p-nitroaniline was added to each of four samples of sewage seed. After twelve days practically all of the original p-nitroaniline had successfully degraded, and at this point further additions of the chemical were made in amounts of 100 mg/l, 200 mg/l and 400 mg/l to each of three samples. Oxygen utilization curves were developed over 74 days. In all three cases, the oxygen curves rose immediately after the extra chemical additions (i.e., the 12th day). The BOD curves were considered normal although protracted for the two situations in which 100 mg/l and 200 mg/l doses had been added. The curve reflecting the addition of 400 mg/l p-nitroaniline demonstrated a different shape. Young and Affleck (5) concluded that there appeared to be no toxic effects up through about 200 mg/l p-nitroaniline. However, at the 400 mg/l level, the oxidation rate was definitely slowed, but "complete" toxicity was not reached, since the p-nitroaniline was eventually degraded (45 to 55 days).

A further test was conducted to determine temperature effects upon biodegradation of para-nitroaniline. Comparison of results obtained at

35°C vs 20°C (95°F vs 68°F) showed rather unexpectedly that there was no degradation of the nitroaniline isomer at 35°C. Apparently all previous testing had been carried out around 20°C. It was also noted that no other series of micro-organisms was capable of adapting to the p-nitroaniline at 35°C throughout the entire test period of 35 days. The sewage portion of the substrate responded in anticipated fashion and showed about twice the degradation rate in going from 20°C to 35°C.

It may be concluded from the above investigations that both ortho- and meta- nitroaniline were not satisfactorily degraded after tremendously long periods of holding. Reasonably large amounts of p-nitroaniline can be biologically treated but careful controls must be exercised and reaction periods are still in the order of many days. It was observed that the yellow color of the p-nitroaniline solution gradually diminished when biodegradation was progressing smoothly.

E. R. Squibb and Sons, Humacao, Puerto Rico

The Squibb Plant planned to segregate their wastes from synthetic penicillin and antifungals production into three main streams: the strong process stream; the weak process stream together with sanitary sewage; and miscellaneous blowdowns plus spent demineralizer regenerants. Company plans stipulated that 99 percent or greater of the organic wastes generated from manufacturing would receive a high degree of treatment (23).

Strong process wastes amounting to about 30,800 kg (68,000 lb) COD/day in an average flow of 44.1 m^3/day (11,800 gpd) were to be sent to storage tanks and continuously fed to a vertical liquid incinerator supplemented by fuel oil. Preliminary test runs had shown that these concentrated wastes could be combusted with a minimal amount of visible plume. However, the wastes originating from the methanol solvent recovery unit, largely still bottoms, were diverted from going to the incinerator because fuel costs for burning this particular waste were thought to be excessively high. They were transferred to the weak process stream (economic considerations overshadowed technical expediency).

The dilute process waste stream amounted to 113 kg (250 lb) COD/day in an average flow of 129 m^3/day (34,000 gpd). This COD apparently does not reflect the addition of the still bottoms mentioned above. These still bottoms demonstrated no acute toxicity but adequate data was lacking in the Squibb report. The stream was to receive biological treatment consisting of waste equalization, activated sludge (probably extended aeration), chlorination, settling and filtration. The effluent would then be sent to a storage tank for cooling tower makeup water. Nutrient addition and pH adjustment, if necessary, would be integrated into biological treatment. Excess sludges will be hauled to land disposal. The biological treatment system was designed for a minimum of 85 percent BOD removal.

The miscellaneous "service waters," amounting to about 132 m^3/day (35,000 gpd), will enter an equalization tank with 2 days' detention, then be neutralized, settled, and pumped to an emergency fire pond as makeup against evaporative losses. Overflow from the emergency pond will be directed to Pridco Ditch serving as the receiving watercourse. Unfortunately, no performance data is available on the Humacao installation, presumed completed, and therefore no judgment can be made concerning the full-scale system.

M/s Indian Drugs and Pharmaceuticals, Hyderabad, India

The Hyderabad, India plant manufactures a variety of synthetic drugs and chemical intermediates. The Indians and Russians in the late 1950's had concurred on a conventional type of treatment facility consisting of equalization, pH adjustment, preaeration (extended aeration), sedimentation, biological filtration with recirculation, secondary sedimentation and lagooning. The primary and secondary settlers and the trickling filter units were planned to be installed in duplicate providing parallel treatment. These plans called for pH adjustment and neutralization of the industrial wastes at the plant site. Domestic sewage would be mixed with the process wastes. Known toxic materials, such as cyanide or arsenic, would be segregated within the plant (30).

A wastewater was simulated in the laboratory based upon the composition of expected factory effluents. The laboratory-scale treatment system was the type described above, and was designed to handle 15 to 19 liters (4 to 5 gal) of synthetic drug waste daily. The trickling filter was studied first. Both the simulated drug waste and 50 mg/l and 100 mg/l of simulated phenolic wastes were applied to the filters. P-aminophenol and p-nitrophenol and sewage were used for preparation of the phenolic waste feed. The full-strength simulated drug waste contained about 2,500 mg/l COD, which was too much for the laboratory filters, so the waste was cut to about 300 mg/l COD. Four runs were made for each of the waste streams. The trickling filtration runs provided 27 to 37 percent COD removals on the drug waste. COD removals on the 50 mg/l phenolic waste ranged from 70 to 87 percent. However, when the phenolic level was increased to 100 mg/l, the COD removal dropped, ranging from 51 to 70 percent. Patil (30) commented that the concentration of phenols in the actual drug waste is in the order of 150 to 200 mg/l, which means very little removal of phenols by trickling filtration. Further, all aromatic compounds which are present in high concentrations in the drug waste will also leave the biological system without being broken down to simpler or less noxious compounds. It was concluded that trickling filtration was not a suitable method to adequately handle the highly complex wastes.

In 1970, Mohanrao (54) described the characteristics and volume of wastes coming from the various manufacturing sectors of the completed Hyderabad, India synthetic drug factory (Tables V-4, 5). Because Sector 8 waste (constituting about 50 percent of the total 568 m^3/day (0.15

mgd) process flows) was fairly dissimilar from the remaining process wastes, strong consideration was given to segregation and separate treatment of the Sector 8 flows. Sulfonilic acid was thought to be the only organic in Sector 8 wastes, and later recovery of acid was deemed possible. Treatability studies were conducted on Sector 8 waste and subsequently on the combined wastes from all other sectors. Presumably because the factory had not yet opened, simulated rather than real wastewater feed was used in all the treatability investigations.

Neutralization of Sector 8 waste was attempted using a 10 percent lime slurry, but sludge settling and separation were poor and there was only minimal removal of BOD, COD and sulfonilic acid. Neutralization and chemical coagulation of wastes from the remaining sectors likewise did not produce significant removals.

Total process waste exclusive of Sector 8 flows was diluted to give 1 and 2 percent waste solutions, which were treated with unacclimated activated sludge for 23 hr. Maximum reductions in BOD and COD were respectively 40 and 32 percent, decreasing on subsequent days and indicating progressive sludge inactivity. This same waste diluted to 0.5 to 8.0 percent (percent volume/volume) was then subjected to acclimated activated sludge, with aeration periods of 23 hr followed by 1 hr of settling. The waste feed concentration could not exceed 7 percent in order to guarantee an effluent containing less than 50 mg/l BOD, and a COD of 250 to 280 mg/l.

With an acclimated sludge and a constant influent BOD of about 1,000 mg/l, the relation between aeration period and MLSS levels vs BOD removal efficiencies at various F/M ratios was developed. Rates of sludge synthesis and settling characteristics were also determined. These results show at a BOD/MLVSS ratio of 0.29 or less, the efficiency of BOD removal approximates 90 percent with an aeration period of 8 hr giving a final effluent BOD of about 100 mg/l. The amount of organic matter in the excess sludges was 87 to 93 percent, and sludge settleability was very good yielding final effluent TSS levels of 30 to 40 mg/l after 20 min. Because of phosphorous deficiency, all of the above wastes were supplemented with dipotassium hydrogen phosphate.

From the laboratory studies, the drug wastewaters are judged amenable to activated sludge treatment but required an absolute minimum of 14 times dilution for efficient organic removals. Information supplied by the factory shows that 2,000 m^3 (0.5 mgd) of domestic sewage containing 100 mg/l BOD, and some 4,000 m^3 (1.0 mgd) of spent condenser wastewater with a BOD about 50 mg/l would be available for diluting the 300 to 350 m^3/day (0.07-0.09 mgd) of process wastes exclusive of Sector 8 flows. Consequently domestic sewage and spent condenser waters were proposed to be used for the dilution of process wastes within biological treatment. This would provide dilution ratios from 17 to 20:1. Process wastes exclusive of Sector 8 flows plus sanitary sewage and condenser waters will be treated via a two-stage high-rate trickling filter recently installed by the factory. This will be followed by an oxidation pond, and the effluent will then pass to the plant sewer. Sector 8 wastes will receive only lime neutralization and sand filtration before finally discharging to the same sewers (54).

Hoffman-LaRoche, Inc. Belvidere, New Jersey

Information on the Hoffman-LaRoche bulk pharmaceutical manufacturing installation at Belvidere, New Jersey was obtained during an NFIC-D visit made on June 29, 1972, and from continuing correspondence regarding the NPDES permit between the Company and EPA, Region II, New York, N.Y. (119). The Belvidere, New Jersey facility initiated operations in 1969 and by June 1972, the plant had approximately 350 employees. Considerable production expansion was experienced during 1972 and 1973, and the Company reported 738 employees in September 1973.

Process Description. In 1972, the Belvidere installation was divided into three process divisions: 1) the Dry Powders Plant; 2) the Sulfa Drugs Plant: and 3) the Vitamin C Complex. Dozens of products are manufactured in the Vitamin Powders plant. A number of chemical intermediates were also included in the above production. Vitamin C manufacturing did not fully come online until late 1972-early 1973. The Company uses at least 80 different raw materials including lead, mercury, palladium and nickel.

According to the 1973 NPDES permit application, vitamin powders are produced by spray drying, spray chilling, and a spray tower process followed by blending operations, yielding 2,040 kg (4,500 lb) daily. The vitamin products require gelatin, vegetable gum, starches, edible waxes and other materials or coatings, covering, and fillers. Since Belvidere directly manufactures both vitamin C and riboflavin, it is assumed that these and other vitamins are converted into vitamin powders and mixes at this same location.

The plant manufactures about 541 kg/day (1,200 lb/day) of hard-shell gelatin capsules. Sulfa drugs consisting of sulfamethoxazole and sulfadimethoxine amount to an average production of 2,490 kg (5,500 lb/day). The sulfa drugs plant is said to present special problems in waste treatment and likely the source of much of the mixed waste salts undergoing special recovery and disposal at Belvidere. Within sulfa manufacturing, at least two inorganic waste streams, spent carbon and filter aid, are separately collected and taken to off-site disposal.

The Riboflavin Manufacturing Process, involving organic synthesis operations, was expected to begin during 1974. The Vitamin C or Ascorbic Acid Manufacturing Process consists of oxidizing glucose to sorbitol, then to sorbose by a fermentation step, through diacetone, and eventually to vitamin C, mostly by organic synthesis procedures. Production of vitamin C in September 1973 was given as 27.2 metric tons (30 tons) per day. Aromatics Manufacturing appears to be producing minor amounts of undesignated complex aromatic organics. Sodium sulfate is a principal product originating from the unique Sodium Sulfate Recovery complex, involving a fluidized bed process and drying of the salt. Various waste streams including selected streams from Sulfa Drug manufacturing are directed to this salt recovery complex. Incoming feed must be carefully controlled to minimize chlorides into the recovery process. The byproduct manufacturing rate was 72.6 metric tons (80 tons)/day sodium sulfate in 1972. Very large amounts of water are evaporated in these operations. Sodium sulfate is said to be marketed for use in pulp and paper manufacturing and detergent chemical manufacturing.

Approval and Startup of Belvidere Plant. Consent was given by the State of New Jersey on July 23, 1968, followed by concurrence of the Delaware Rier Basin Commission (DRBC) in Sept. 1968 for industrial waste treatment facilities at Hoffman-LaRoche, Belvidere, N.J. Besides sulfa drugs and vitamin C manufacturing, the establishment was said to include an animal testing farm for basic research, although the latter function probably was not constructed. The proposed treatment facilities were to provide screening, waste equalization and pH adjustment, chemical flocculation and settling, activated sludge aeration with final settling, followed by holding lagoons and chlorination. The design flow was cited as 3,780 m^3/day (1.0 mgd). Excess biological sludges were to be lagooned and dried in open beds, but only as a temporary measure. A fish aquarium tank was to be installed in the plant laboratory and would receive treated effluent continuously as a monitor on toxicity.

The initial flows of sanitary sewage and industrial waste were not expected to exceed an average of 150 m^3/day (40,000 gpd) with a maximum BOD for the raw wastes of 185 mg/l. This loading was equal to only 28 kg (62 lb) BOD/day. Under full operation, the raw wastes at the design flow of 3,780 m^3/day (1 mgd) were expected to have a BOD of 1,900 mg/l and a TSS of 1,000 mg/l. These values are equivalent to daily loadings of 7,190 kg (15,860 lb) BOD/day and 3,790 kg (8,350 lb) TSS/day. The treatment plant design approved by the Delaware River Basin Commission specified effluent loadings of 50 mg/l BOD = 190 kg (417 lb)/day BOD and 20 mg/l TSS = 76 kg (168 lb)/day TSS. The design conditions provided for BOD removals of 97.4 percent and TSS reductions of 98.0 percent.

In June 1972, the Company reported a waste flow averaging about 1,020 m^3/day (0.27 mgd) and containing a raw wasteload of about 5,440 kg (12,000 lb) BOD/day. Startup of the vitamin C complex was anticipated during the latter half of 1972 at which time the raw wasteload was expected to reach to 13,600 kg (30,000 lb) BOD/day. These Company figures are noted as being much higher than design estimates previously given to the State and the DRBC in 1968. By Sept. 1973, the Company on its revised permit application increased its flow estimate to 6,100 m^3/day (1.6 mgd) together with a maximum flow of 7,950 m^3/day (2.1 mgd). This compares to the design flow estimate of 1.0 mgd given in 1968.

The treatment works were a multifunction system. As of June 1972, total construction expenditures were estimated at about \$2.6 million. The Company in 1970 had estimated that full system costs for abatement of water, air and solids waste pollution would eventually approximate \$4.0 million. Waste streams include industrial and sanitary flows, water treatment plant sludges, regenerants, and various blowdowns all directed to treatment.

Raw wastes entered the treatment plant through a barminuter and bar screens into a 284 m^3 (75,000 gal) preclarifier which was integral with a 2,780 m^3 (1 million gal) equalization basin. Very little solids accumulation was noted in these first two holding basins. The equalization basin is equipped with two turbine type surface aerators, operating at 25 hp each. Full load on each aerator is 100 hp. No chemicals are added to this side of the treatment plant. The TSS in the equalizing basin were only about 200 mg/l, but waste loads during this period were only about one-fourth of full normal loads. The equalized wastewaters passed through a parshall flume, received pH adjustment, and entered a 17 m (55 ft) diameter x 3 m (10 ft) deep flocculator-clarifier with a 673 m^3 (178,000 gal) capacity. This chamber was not in full use during June 1972. The wastewaters then proceeded to an aeration basin 6 m (20 ft) deep by 36.6 m (120 ft) long by 12 m (40 ft) wide. The aeration basin had common wall construction with a second basin of similar size being used as an aerobic sludge digestion tank. A 7.6 m (25 ft) diameter tank of 135 m^3 (35,700 gal) capacity was available as a sludge thickener but was not in use. Aeration basin effluents were routed to a secondary clarifier which was identical in size to the flocculator-clarifier previously described. Secondary clarifier effluents were passed through two 3,780 m^3 (1 million gal) shallow oxidation ponds (no artificial aeration), then chlorinated before final discharge to the Delaware River. Excess biological sludges were being taken to experimental sludge drying beds with the dried sludge cake believed to be ultimately carted away to landfill.

Testing was conducted for BOD, COD, TOC, pH, conductivity, dissolved oxygen, color, chlorides and temperature. The live continuous flow-through bioassay aquaria used fathead minnows as the test species. Three aquaria were used, one serving as the control (also holding extra fish), the second containing only Delaware River water with fish, and the third stocked with test fish containing treated effluents diluted 200-fold with Delaware River water.

By Sept. 1973, the Company declared it was no longer possible to consistenty attain the effluent design loads of 1968. The permit application of Sept. 14, 1973 lists treated average discharge loads for the single outfall 001 as follows:

Component	Load	
	(kg/day)	(lb/day)
BOD	260	574
TSS	435	960
COD	1,324	2,920
TDS	17,900	39,500
NH_3, N	5	11
PO_4, P	10	23
TOC	422	930
Sulfates	454	1,000
Chlorides	998	2,200
Aluminum	0.3	0.6

Component	Load	
	(kg/day)	(lb/day)
Iron	0.5	1.2
Lead	0	0
Nickel	0	0
Sodium	1,840	4,060
Zinc	2.4	5.3
Oil/Grease	0	0
Phenolics	0	0
Fecal Coliforms	--	5/100 ml

Current raw wasteloads were not available. Nevertheless, minimum reductions can be calculated using raw waste values of 7.2 kkg (15,860 lb)/day BOD and 3.8 kkg (8,350 lb)/day TSS given as design conditions in 1968, and a BOD raw waste loading of about 13.6 kkg (30,000 lb)/day reported for the end of 1972. The BOD removals, based respectively on 7.2 kkg (15,860 lb)/day and 13.6 kkg (30,000 lb)/day raw loads, are 96.4 percent to 98.1 percent. The TSS removal, based on 3.8 kkg (8,350 lb)/day, is 88.5 percent.

The above calculations are thought to represent minimum waste reductions, and therefore typical removals through the treatment systems are presumed to be about 97.5 percent BOD and at least 90 percent TSS. It is noted from the Sept. 1973 permit application data that ammonia and organic nitrogen loads in the final effluents are exceptionally low.

The COD parameter is always considered important in properly characterizing pharmaceutical wastewater but also EPA Region II recently asked Hoffman-LaRoche to conduct a study of the sources of TOC in the discharge. This study was not only intended to identify TOC components but also to set the basis for removal of such compounds from the discharge and enable effluent limitations under the NPDES permit. The superiority of COD vs TOC or TOD is undergoing evaluation. The addition of TOC to continuously collected BOD and COD information by the company would seem very desirable. Review of the literature indicates that certain reduced inorganic ions can be oxidized under the COD test giving abnormally high results. The dichromate oxidation of sulfites, sulfides, nitrogen and ferrous iron was suggested. Ongoing study by Hoffman-LaRoche tentatively shows that refractory-type compounds are resistant to decomposition in the COD and BOD tests, whereas they may be measured by the TOC analysis. The opposite may also be true.

Assuming in the study that ultimate BOD is about 90 percent of theoretical oxygen demand and BOD_5 is about 48 percent BOD_{ULT}, the ratios below were developed.

$$\frac{BOD_5}{TOC} = \frac{O_2}{C} = \frac{32}{12} \text{ X } (0.9 \text{ X } 0.48) = 1.15$$

$$\frac{COD}{TOC} = \frac{O_2}{C} = \frac{32}{12} = 2.66$$

In turn, these ratios were compared to the ratios derived on the wastes entering and leaving the Belvidere treatment system during 1972.

	BOD/TOC	COD/TOC	COD/BOD
Influents	0.64 - 0.88	2.32 - 2.83	3.13 - 4.35
Effluents	0.03 - 0.05	2.00 - 2.83	33.3 - 142.3

Evaluation of this data spectrum shows that:

1. The BOD/TOC ratios from the treatment system were less than calculated values and dropped considerably with increasing waste stabilization.

2. The COD/TOC ratios from the treatment system approximated the calculated values and did not vary significantly between the influent and the effluent.

3. The COD/BOD ratios for treated effluents were very high.

The Company comments that a nonbiodegradable residue will probably remain in the effluents even after biological treatment. Even a well-oxidized secondary sewage treatment plant effluent is shown to contain 10 mg/l BOD, perhaps 10 to 20 mg/l TOC, and 60 mg/l COD. The Company thought that somewhat more material might be present in the effluents than in the influents that would be slightly less amenable to dichromate oxidation (COD/TOC ratios). However, the data collected does not warrant this conclusion. The presence of nonbiodegradable materials and/or inorganics were said to contribute to the relatively low BOD/TOC ratios. More data was necessary, and Hoffman-LaRoche indicated that other analyses such as gas chromatography, thin-layer chromatography, and spectrophotometric techniques will probably be necessary to determine specific nonbiodegradable and inorganic fractions (119).

Known air pollution control measures at the Belvidere facilities include cyclones with water sprays serving the Vitamin Powders plant together with baghouse units and a wet scrubber on the vitamin spray dryer exhaust. Belvidere has centralized solvent recovery, but it also collects large quantities of nonrecoverable or nonuseable solvents and conveys them to offsite incineration or landfill.

Fermentation/Synthesized Organic Chemicals

Abbott Laboratories, North Chicago, Illinois

The Abbott installation represents a large pharmaceuticals manufacturing plant with approximately 6,000 employees operating on a 3-shift, 24 hr/day, 7 day/week continuous schedule. They have extensive fermentation and antibiotic manufacturing facilities. Two of the most important antibiotics at Abbott in past years have been erythromycin and penicillin. Of the hundreds of fine chemicals and other medicinals made by Abbott, major types include the sedatives, diuretics, the antihypertensives, anticoagulants, anticonvulsants, laxatives and antidandruff preparations. Abbott also produces animal feed supplements, intravenous solutions and associated equipment, irrigation solutions, vitamin preparatons, cough medicines and a host of other health products. At least one "biological insecticide" was manufactured there in 1972. They conduct highly varied processing of synthesized organic materials including drug preparation, formulation and packaging operations. Furthermore the Company maintains a small manufacturing, packaging and research center located at Abbotts Park near North Chicago. This center is engaged in the production of radiopharmaceuticals.

Early Production and Waste Treatment. The plant, less than one-half mile from Lake Michigan, draws its water intake from and also returns treated effluents to the Lake. Over the years, because of the magnitude and complexity of the waste streams, it has been desirable and also necessary for the Company to operate its own waste treatment works. Starting with modest penicillin production during the early 1940's, fermentation activities grew steadily from the 1940's through the 1960's, with rapid expansion occurring through the 1960's. Although heavily engaged in antibiotics production via fermentation, there is considerable activity in the manufacture of fine chemicals through multiple-step chemical reactions. In the middle-1960's, fermentation wastes were said to contribute about 80 percent of the organic matter in the combined Abbott process waste streams.

Waste treatment in the early 1940's consisted of neutralization, lagooning and chlorination. An activated sludge plant was constructed in 1953 which consisted of twin primary tanks, twin aeration tanks, settling tanks, chlorination, sludge filtration and land disposal. Design capacity of this plant operating at 90 percent BOD removal was 2,720 kg (6,000 lb) BOD/day raw waste loading within an average flow of 1,890 m^3/day (0.5 mgd). The primary tanks were 76 m^3 (20,000 gal), the aeration tanks were 1,140 m^3 (300,000 gal), and the secondary settlers both had a 150 m^3 (40,000 gal) capacity (22,56,103). Sanitary effluents, spent process streams, and storm flows were segregated. Sanitary flows were sent to the nearby municipal treatment plant; cooling waters were released to the lake without treatment; and process wastes were received into the biological treatment system.

Turbine Mixer Aeration. In 1957, a pilot plant was built to thoroughly investigate the merits of turbine mixer aeration which promised up to 15 times higher allowable BOD loadings per unit volume of aeration tank than previous processes. The process wastes from Abbott's manufacturing operations were averaging 2,400 mg/l as predominately soluble BOD. The pilot plant using sparged turbine mixers demonstrated power consumption as low as 0.34 kwh/lb of BOD removed compared to 0.6 kwh for conventional municipal treatment plants, and 0.56 kwh per lb BOD removed for the Abbott plant previously using hydraulic ejectors. Whereas conventional municipal treatment works employing activated sludge were being designed at BOD loadings around 0.5 kg/m^3 (30 lb) BOD/1,000 ft^3 of aeration volume, the Abbott pilot plant showed the ability to handle loads up to 7 kg/m^3 (440 lb) BOD/1,000 ft^3 concurrently giving 80-90% reductions. This led to replacement of existing aeration equipment with sparged turbine mixers by Abbott in 1958. Also, the primary settlers were modified into sludge flotation units. These units produced 6 percent sludge solids from a 1 percent feed and served successfully to concentrate activated sludge (22, 56, 103).

For full-scale sparged turbine mixer aeration, a total of 300 hp mixer capacity was incorporated into the single 1,250 m^3 (330,000 gal) aeration basin. The turbine mixer was intended to operate at a 90 percent efficiency. The aeration tank was subdivided into three compartments, each 11 m (36 ft) long by 10 m (32 ft) wide by 3.8 m (12.5 ft) deep. Each chamber had two turbine mixers. The pre-existing system of two aeration tanks was reduced to one tank, and the second was converted to a waste equalization basin. The treatment plant provided for neutralization of raw wastes, flow equalization in the 1,250 m^3 (330,000 gal) tank, followed by a three-compartment activated sludge basin, secondary settling and chlorination. Flows progressed through the three activated sludge compartments in series. A flotation thickener served to concentrate underflows from the secondary clarifier for return to the aeration basin or for ultimate disposal.

When all three aeration compartments were thoroughly agitated, good separation of solids in the secondary settler could not be attained because the mixed liquors were highly gasified. Consequently, the two mixers in the last aeration compartment were turned off and the air was reduced. This change considerably improved sludge settling. The last compartment was used more for degasification than for aeration of the mixed liquors. Sustained full-scale operation of the activated sludge basin under the conditions outlined above permitted BOD loadings in the range of 7.2 to 8.8 kg/m^3 (450 to 550 lb/1,000 ft^3) tank capacity/day. BOD reductions of 75 to 85 percent were obtained. Air requirements averaged about 13,750 m^3/kg (220 ft^3 air/lb) BOD applied, and about 20,000 m^3/kg (320 ft^3/lb) BOD removed. Power needs in removing BOD were quite low, averaging about 0.41 kwh/lb BOD (6, 55).

Special Laboratory Programs. To provide ample laboratory support of the treatment plant, a series of special lab procedures and programs were developed by Abbott. These included a shaken flask test, a sludge activity test, bench-scale activated sludge units designed to provide answers on long-term treatment responses, and routine analysis of the raw wastes for nutrients and inhibitory components (35).

The shaken flask test was designed to give quick indications on the amenability of new wastes to the activated sludge system. It was necessary to know whether occasional poor treatment performance was due to decreased sludge activity, to a substrate having low oxidation potential, or to some inhibitory component being present. The shake test uses a 500 ml flask receiving 100 ml of substrate together with 2,500 to 5,000 mg/l of activated sludge obtained from the treatment system. The flask is shaken at 325 cpm for a prescribed period, samples are withdrawn and analyzed, and percent waste removals are calculated. The test showed that a certain cyclic amine being disposed of intermittently was inhibitory to activated sludge when present in amounts greater than 100 mg/l. This data prompted the Company to improve recovery of the cyclic amine by adding a stripping column and closely regulating the rate of release of this compound. The flask test was also utilized to determine the effect of temperature upon BOD reduction and to assess the minimum temperature level at which steam injection and/or activated sludge reseeding was advisable. The tests were run for periods of 1, 7 and 24 hr. Drops in activated sludge treatment efficiencies were observed at temperatures of 18 to 24°C (65 to 75°F) or below, and corrective measures were implemented.

The sludge activity test told whether a low BOD reduction may be due to the raw waste having a low oxidation rate, or the sludge itself having poor activity. For relatively low oxidation of the waste, consideration can be given to nutrient addition, adaption of the sludge to the waste, or isolation and/or removal of the particular process waste stream. Bench-scale activated sludge units were used in initial attempts to discover if weekend shutdowns at the main manufacturing plant would have a significant impact upon waste treatment (35).

The 1960's. In 1964, a large degassing and settling tank was added to improve the solids separation in the secondary clarifier. The secondary settler consisted of a standard peripheral feed circular tank. The degasification chamber was added to the outer circumference of the settler at the feed end. This operation was designed with drilled pipe air sparging for the purposes of promoting flocculation and enhancing the settling characteristics of the activated sludge clumps.

Also in 1964, a change was made from chlorination to pasteurization of the treated process effluents. In this unique pasteurization process, the turbine exhausted into a newly added barometric condenser with the former chlorine contact chamber becoming the hot well. Steam at 5 to 10 psig was readily available from plant operations, and was reused in driving the condensing steam turbine. The exhaust steam, in turn, was condensed in the barometric condenser with the treated wastewater effluent serving as the coolant. In this process, the effluent wastewaters were heated up to 65 to 71°C (150 to 160°F) and held for 30 min in the hot well, thereby completing the pasteurization process (22).

In 1965, more aeration of the sparged turbine type was added to existing facilities. Expansion of fermentation activities (primarily erythromycin) was steadily occurring through the 1960's with the largest additions in 1966-67. This caused a major re-evaluation of overall waste handling. Fermentation wastes were said to contribute about 80 percent of the organic matter in the combined process waste streams. The plant decided to recover spent fermentation broths and sell them as animal feed supplements for these reasons:

1. Only spent beer drying could meet the stringent effluent limitations expected in the future.
2. All materials dried would receive the equivalent of 100 percent treatment.
3. Efficiency of the existing treatment system would be improved because of reduced BOD load to the aeration tanks and lower hydraulic load placed on final clarification
4. There would be considerably less "excess" activated sludge generated for final disposal
5. A marketable product would be created
6. The odor control system designed for the drying operations could be, and was subsequently expanded to include the existing activated sludge plant, thereby solving another problem.

Processes selected for the drying of spent beers consisted of:

1. Isolation and separate collection of the spent beer streams
2. Concentration of the spent beer streams from 4 to 5 percent solids up to 30 to 35 percent solids via triple-effect forced circulation evaporators
3. Subsequent drying of the concentrates by steam-heated drum dryers
4. Bulk solids storage, packaging and marketing
5. Necessary odor control

One of the more critical aspects of the beer drying operations was odor control which constituted a major undertaking. Incineration was considered the most feasible and effective method of destroying odors, although carbon absorption, wet scrubbing, chemical oxidation, odor masking chemicals, and tall stack dispersion were evaluated. The possible incineration schemes contemplated were straight incineration at the site, catalytic incineration at the site, and ducting of the odorous air streams over and into the main plant steam boilers. These streams would in effect be used as combustion air supply. The latter system proved to be the most economical approach. The duct was designed in such fashion to allow for future additional connection of the exhaust air from all the fermenters and full connection from the waste treatment plant. The combined odorous air stream was to serve as combustion air supply to three 60 kg/cm^2 (850 psig) steam boilers. This air stream would be oxidized at boiler temperatures of 980°C (1,800°F) to 1,090°C (2,000°F). The ducting system ran 365 m (1,200 ft) in length with a diameter varying from 122 to 137 cm (48 to 54 in).

It was reported shortly after the incinerator ducting system had been installed in late-1967 that not only were the fermenter exhausts hooked up but also the activated sludge tanks were enclosed and their exhausts were likewise connected to the main ducting system. Odors from the degassing chambers and sludge holding tanks were handled similarly (22).

Transition, 1969-71. Additional waste abatement measures from 1969 through 1971 included:

1. Two more aeration tanks
2. A second combination degassing and secondary settling tank
3. A 67 percent increased waste equalization capability
4. A centrifuge system for sludge removal
5. An electrostatic precipitator and necessary equipment on the main boilers to allow for burning of waste sludge
6. Surface condensers to replace most barometric condensers
7. Major process and storm sewer renovations, extension and modifications

Peripheral waste recovery and abatement programs were: solvent recovery/recycle/incineration; ammonia recovery; accidental spill control; and solid waste disposal-recycle operations.

Separate solvent recovery systems were installed, and in 1973, about 114 m^3/day (30,000 gpd) of aniline, benzene and amyl acetate were being recovered for reuse. Some mixed solvents are collected for sale and some are incinerated in a smoke-free solvent burner.

Ammonia is recovered in dilute form from at least one of the chemical manufacturing operations. It is then concentrated and sold in bulk as fertilizer. The spill control program at Abbott incorporated unusual design in storage units, installation of extensive diking and curbing, and sewer separation. Contamination throughout the separate sanitary, process, and cooling water sewer networks is monitored and recorded to quickly pinpoint leaking equipment, faulty sewers, and process irregularities (103, 109).

New Wastewater Treatment System. Presently, Abbott has three separate wastewater drainage systems. About 1,885 m^3/day (0.5 mgd) of sanitary sewage and cafeteria wastes are discharged to the North Shore Sanitary District North Chicago Sewerage Works. Spent cooling waters are collected, chlorinated, and discharged more or less without treatment. This flow averages 55,600 m^3/day (14.7 mgd). The Company reports that only cooling waters enter this sewer. However, as of 1972, the sewer was also collecting drips and condensates from the first-effect spent fermentation beer evaporator, boiler blowdowns, some floor drainage, packing gland coolants, liquid effluents from wet scrubbing of air streams, barometric condensates from the spent broth evaporation system, and undefined tank and miscellaneous washings (103, 119).

As of 1972, the Company was able to meet all imposed effluent criteria by the State and local authorities. The treatment works as of 1973 had a reported hydraulic capacity of about 3,780 m^3/day (1.0 mgd) and an organic loading capability of 13,600 kg (30,000 lb) BOD daily with greater than 90 percent BOD removals (16, 103, 119). This system is described as follows:

1. Raw Waste Handling - Fermentation and chemical wastewaters are passed through a fine bar screen, the flows and pH are recorded, and the wastes enter a wet well. The pH of the raw wastes can vary from 3 to 13 in a few minutes. The wastes are neutralized and pumped from the wet well to the equalization basins.

2. Equalization - Two equalization basins are available, each 1,890 m^3 (500,000 gal), providing an effective capacity of 3,600 m^3 (960,000 gal) and giving 1.0 to 1.5 days detention at average flow rates. One of these basins is divided into three compartments and can be used for the segregation and partial storage of potentially toxic or inhibitory chemical compounds. Each basin is equipped with three 25 hp mixers to provide necessary agitation during equalization and holding.

3. Aeration - The activated sludge aeration tanks consist of six 378 m^3 (100,000 gal) compartments. Four of the compartments are equipped with two 50 hp sparge air turbines, and the two remaining compartments each have a single 50 hp unit. A total of 500 hp is available in the aeration basins. Waste retention time is about 24 hr, excluding the sludge return volumes. Operating temperatures are closely controlled at 38°C + 2°C, the F/M ratio is maintained at about 0.25, and the MLVSS is considered optimum at 8,000 to 12,000 mg/l. All the equalization basins and the activated sludge chambers are enclosed by a flat slab concrete covering. As described previously, a ducting system continuously conveys the odorous exhausts from the equalization and aeration chambers to the central boiler house for incineration.

4. Degassing - The mixed liquors leaving the aeration tanks are heavily entrained with fine air bubbles. Since this greatly inhibits subsequent solids separation, degassing is necessary. The waste stream enters a common wall degassing/launder chamber which surrounds the settler and has a capacity of about 625 m^3 (165,000 gal). Diffused air at the bottom of the degassing chamber accelerates the release of entrained gases and breaks down the foamy layer. Mean residence time in the chamber is about 8 hr at high hourly flow rates.

5. Final Settling - Two 18 m (60 ft) diameter secondary clarifiers can provide a surface overflow rate of 1.3 $m^3/day/m^2$ (180 gsfd). Sludge return rates of up to 15,100 l/min (4,000 gpm)

are possible to the aeration basins, although sludge return is usually maintained at 500 percent of the effluent rate. Excess sludges are sent to a pair of sludge centrifuges handling about 570 l/min (150 gpm).

6. Pasteurization - Pasteurization at 66°C (150°F) and 20 min wastewater detention offers three distinct advantages over chlorination: a) a more positive coliform control can be maintained; b) a potential safety hazard that chlorine presents can be eliminated; c) lower operating cost. The chlorine equipment was retained on an emergency standby basis.

7. Spent Beer Recovery - Spent beers are concentrated via multiple-effect evaporators to a 30 percent solids concentration. The resulting thick syrup is shipped in tank cars and sold as an additive in chicken feeds. Excesses are incinerated in plant boilers. Although Abbott had previously installed driers, operating problems were experienced and drying was discontinued.

Abbott Labs reported achieving an average overall BOD removal of 94 percent throughout 1971, 95 percent in 1972, and 96 percent removal through the early part of 1973. The spent beer recovery program was judged largely responsible in achieving BOD removals greater than 95 percent.

In 1972, the process wastes averaged 2,270 m^3/day (600,000 gpd) and had a population equivalent of about 100,000 persons ~6,800 to 9,100 kg (~15,000 to 20,000 lb) BOD/day. Waste characteristics were given as follows (103):

Parameter	Flow (m^3/day)	Flow (mgd)	BOD (mg/l)	TSS (mg/l)	TDS (mg/l)	pH
Chemical wastes	990	0.262	2,520	510	5,690	5.4
Fermentation Wastes	1,180	0.312	3,620	1,660	3,590	6.7
Combined	2,180	0.575	3,120	1,140	4,620	6.1

Abbott calculates that their recycling and recovery operations in 1972 were responsible for reclaiming waste materials having a population equivalent of about 300,000 persons ~23,000 to 27,000 kg (~50,000 to 60,000 lb) BOD/day. Quality data on the combined treated process plus cooling water flows after final chlorination for July through Dec. 1972 are shown below:

Parameter	Actual Concentration (mg/l)	1972 State Effluent Standards (mg/l)
BOD	16	20
TSS	20	25
TDS	400	750
Phosphorous, P	0.6	1.0
Phenolics	0.02	0.3
Coliforms, counts/100 ml	11	400
Mercury	0.0003	0.0005
pH	7.5 units	5-10 units
Flow m^3/day (mgd)	56,800 (15.0)	

Waste treatment performance data compiled from Monthly Summary Sheets submitted by the Company to the State are given in Tables VIII-1 and VIII-2 for Jan. 1972 through Dec. 1973. Steadily improving waste removal efficiencies are apparent. The overall BOD and TOC removals for 1972 averaged 94.6 percent and 86.0 percent, respectively. In 1973, the average BOD and TOC reductions were 96.7 percent and 83.0 percent, respectively. In some months in 1973, BOD reductions approached and even exceeded 98.0 percent. If the spent fermentation beers going to the evaporators are considered an equivalent part of the process waste loads, average BOD reductions for 1972 and 1973 would be 97.8 percent and 98.7 percent respectively for the two years. These recovered beers are thought to have a BOD load potential of 9,070 kg (20,000 lb) BOD/day or greater. Percentage removals of total suspended solids were below desired levels, although average removals were still in the 71 to 74 percent range. Significant carryover and entrainment of gases within the mixed liquors leaving the aeration basins is likely yet occurring. If spent fermentation beers were accounted for as part of the TSS raw waste loads, reduction of equivalent raw loads may have easily exceeded 80 percent.

The technical feasibility of incinerating excess biological sludges in the coal-fired boilers had been previously demonstrated but volumes to be disposed of by this means were originally too large. A continuous feed disk nozzle centrifuge consistently produced a 5 percent concentrated sludge feed at 378 m^3 (100,000 gal)/week to the boilers. Based upon a rate of 30,000 m^3 (7.8 million gal) of sludge being incinerated yearly, Abbott calculated incremental costs as $219,300 or $28.10 per 1,000 gal of sludge incinerated. This boiler system operating at 980°C (1,800°F) or above was found to be a most efficient method for eliminating both process odors as well as the sludges (16,103,119).

The summary data show that from 1972 to 1973 hydraulic and organic loadings increased from 8 to 16 percent, and a similar trend may be likely in 1974. This indicates that production may be exceeding the available capacity of the treatment works. Ammonia and phosphate loads in the combined effluents are quite low. Mercury may be approaching marginal conditions and arsenic concentrations during certain months are

Table VIII-1

Influent and Effluent Loadings Through Biological Treatment Works

Abbott Laboratories, North Chicago, Ill., 1972-1973

Month	Flow		BOD					TOC					TSS				
			Influent		Effluent		Red[a/]	Influent		Effluent		Red[a/]	Influent		Effluent		Red[a/]
	(m^3/day)	(mgd)	(kg/day)	(lb/day)	(kg/day)	(lb/day)[b/]	(%)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(%)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(%)
1972																	
Jan.	2,020	0.534	5,770	12,730	283	625	95.1	-	-	-	-	-	2,390	5,270	676	1,490	71.7
Feb.	2,180	0.577	5,790	12,760	249	549	95.7	3,220	7,110	390	852	88.0	2,330	5,140	380	838	83.7
Mar.	2,080	0.549	6,530	14,400	340	751	94.8	3,210	7,075	493	1,086	84.7	2,300	5,080	713	1,571	69.1
Apr.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
May	2,240	0.593	8,300	18,310	525	1,158	93.7	4,140	9,120	552	1,217	86.7	2,230	4,915	1,100	2,435	50.5
June	2,340	0.619	7,150	15,760	365	806	94.9	4,170	9,200	548	1,209	86.9	2,350	5,190	708	1,560	69.9
July	2,100	0.555	7,120	15,700	411	908	94.2	3,810	8,410	498	1,098	86.9	3,100	6,830	563	1,241	81.8
Aug.	2,310	0.610	7,340	16,190	489	1,079	93.3	4,680	10,320	503	1,110	89.2	3,300	7,270	654	1,441	80.2
Sept.	2,340	0.619	8,650	19,070	466	1,028	94.6	4,960	10,930	810	1,737	83.7	2,690	5,925	645	1,421	76.0
Oct.	2,160	0.570	6,590	14,530	412	909	93.7	4,470	9,860	693	1,527	84.5	2,140	4,715	969	2,136	54.7
Nov.	1,930	0.511	5,950	13,120	267	588	95.5	3,500	7,710	514	1,134	85.3	2,220	4,890	783	1,727	64.7
Dec.	2,020	0.534	4,900	10,810	216	477	95.6	3,140	6,925	522	1,150	83.4	2,330	5,140	527	1,163	77.4
Avg.	2,160	0.570	6,740	14,850	366	807	94.6	3,930	8,665	552	1,217	86.0	2,490	5,490	702	1,547	71.4
1973																	
Jan.	2,250	0.594	6,670	14,710	272	600	95.9	3,790	8,365	632	1,393	83.3	2,680	5,905	652	1,438	75.6
Feb.	2,520	0.666	8,020	17,680	487	1,073	93.9	5,020	11,060	1,050	2,312	79.1	2,740	6,052	1,030	2,273	62.4
Mar.	2,270	0.599	6,970	15,370	236	520	96.6	4,610	10,170	610	1,345	86.8	2,470	5,435	426	940	82.7
Apr.	2,400	0.635	7,770	17,120	156	344	98.0	4,550	10,025	627	1,383	86.2	1,740	3,830	555	1,224	68.0
May	2,490	0.658	7,790	17,165	139	307	98.2	4,820	10,620	740	1,631	84.6	2,080	4,580	625	1,378	69.9
June	2,430	0.643	8,490	18,710	204	451	97.6	4,830	10,655	696	1,535	85.6	2,510	5,530	545	1,202	78.3
July	2,420	0.639	6,860	15,120	184	405	97.3	4,290	9,450	779	1,717	81.8	2,640	5,380	796	1,754	67.4
Aug.	2,420	0.640	8,200	18,070	182	401	97.8	4,540	10,005	681	1,501	85.0	2,450	5,400	370	817	84.9
Sept.	2,540	0.672	8,420	18,570	295	651	96.5	4,570	10,080	865	1,907	81.1	2,540	5,600	552	1,217	78.3
Oct.	2,720	0.719	6,640	14,640	204	450	96.9	4,200	9,250	721	1,590	82.8	2,840	6,250	509	1,122	82.0
Nov.	2,820	0.746	5,910	13,035	155	342	97.4	3,730	8,235	675	1,488	81.9	2,220	4,895	511	1,127	77.0
Dec.	2,670	0.705	6,010	13,260	411	906	93.2	3,810	8,395	880	1,941	76.9	2,390	5,265	1,020	2,241	57.4
Avg.	2,500	0.660	7,310	16,120	244	538	96.7	4,400	9,690	750	1,645	83.0	2,420	5,345	633	1,395	73.8

[a/] Reduction

[b/] Monthly BOD concentrations leaving treatment plant during 1973 were in the range of 56 to 193 mg/l; corresponding TSS levels were 153 to 409 mg/l. Monthly concentrations for total plant effluents during 1973 were 9 to 20 mg/l for BOD averaging 13 mg/l; corresponding TSS values were 10 to 53 mg/l averaging 27 mg/l.

Table VIII-2

Nutrient and Trace Contaminants
Treated Process Combined with Cooling Water Discharges
Abbott Laboratories, North Chicago, Ill., 1972-1973

Month	Flow		Phosphates as P			Ammonia as N			Arsenic	Phenolics	Cyanides	Selenium	Mercury
	(m^3/day)	(mgd)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(mg/l)	(mg/l)	(ppb)	(ppb)
1972													
Jan.	-	-	-	-	-	-	-	-	0.7	-	-	-	-
Feb.	50,500	13.34	0.9	45	100	2.8	145	320	0.6	0.05	0.004	< 0.5	3.0
Mar.	52,300	13.82	0.9	47	104	2.6	136	300	0.5	0.02	0.002	< 0.5	< 0.5
Apr.	-	-	-	-	-	-	-	-	-	-	-	-	-
May	67,200	17.76	0.9	60	133	4.1	276	608	0.3	0.03	0.009	0.9	0.3
June	71,100	18.78	0.8	57	126	4.9	348	768	0.4	0.06	0.008	1.3	-
July	67,900	17.95	0.6	41	90	3.0	204	450	0.2	0.01	0.004	1.4	-
Aug.	82,000	21.66	0.6	51	112	3.2	262	578	0.1	0.03	0.001	0.9	-
Sept.	52,200	13.79	0.6	31	69	2.8	146	322	0.2	0.02	0.003	3.2	< 0.2
Oct.	52,000	13.74	0.6	31	69	1.8	93	206	0.1	0.01	0.005	< 0.5	< 0.3
Nov.	44,700	11.80	0.9	40	89	2.6	116	256	0.2	0.03	0.005	4.1	< 0.2
Dec.	41,400	10.93	0.9	37	82	1.5	62	137	0.3	0.04	0.003	4.4	-
Avg.	58,100	15.36	0.8	44	97	2.9	179	395	0.4	0.04	0.004	~ 2.0	~ 0.7
1973													
Jan.	46,300	12.24	1.1	51	112	3.0	139	306	0.2	0.02	0.004	4.9	0.1
Feb.	50,200	13.26	1.1	55	122	1.8	91	200	0.2	0.02	0.003	4.6	-
Mar.	57,200	15.12	0.8	46	101	1.8	103	227	0.4	0.01	0.005	2.7	0.2
Apr.	64,900	17.14	0.6	39	86	3.7	240	529	0.3	0.01	0.006	2.2	0.1
May	77,100	20.37	0.6	46	102	5.4	416	918	0.3	0.04	0.004	4.6	< 0.1
June	94,700	25.02	0.5	47	104	1.9	180	397	0.3	0.01	0.005	3.6	0.1
July	94,000	24.83	0.4	38	83	1.4	131	290	0.3	0.01	0.005	2.3	< 0.1
Aug.	97,900	25.87	0.3	29	65	1.8	176	389	0.3	0.01	0.007	3.8	< 0.1
Sept.	72,600	19.19	0.2	15	32	2.1	152	336	0.2	0.01	0.007	2.3	< 0.1
Oct.	64,700	17.11	0.3	19	43	1.4	91	200	0.1	0.01	0.005	2.7	0.2
Nov.	51,100	13.50	0.5	25	56	2.3	117	259	0.3	0.01	0.008	4.1	0.1
Dec.	41,700	11.01	0.6	25	55	0.9	38	83	0.2	0.01	0.006	2.7	< 0.1
Avg.	67,800	17.90	0.6	36	80	2.3	156	345	0.3	0.01	0.005	3.4	~ 0.1

higher than desirable. Arsenic should be maintained between 0.1 and 0.2 mg/l, or lower.

The Abbott waste treatment works represents a multimillion dollar installation. The spent beer recovery system was indicated as having an additional fixed cost of $2.0 million or more. Annual operation costs for the waste treatment plant are said by the Company to approximate $1.2 million which prorates to $1.20 to 1.30/m^3 ($4.50 to $5.00 for each 1,000 gal) of process wastes treated. Of this amount, about $0.50 is for the depreciation of existing treatment facilities.

In view of increasingly tight effluent requirements by the State of Illinois for discharges into Lake Michigan, the Company as of 1971-72 made plans to connect their treated waste effluents to the advanced waste treatment plant to be built by the North Shore Sanitary District at Gurnee, Ill. Abbott intends to continue full operation of their waste treatment facilities before discharge of the treated effluents to the District. The Company will also continue release of the spent cooling waters into Lake Michigan. The Gurnee plant as of 1973 was designed to produce an effluent of 10 mg/l BOD and 12 mg/l TSS for eventual discharge into the Des Plains River. State effluent criteria for releases into Lake Michigan by 1975 will be 4 mg/l BOD and 5 mg/l TSS. It is noted that the combined Abbott plant discharges in 1973 averaged 13 mg/l BOD and 27 mg/l TSS (16, 103, 119). The Gurnee plant was originally scheduled to be completed in 1973 but apparently certain delays have occurred.

Wyeth Laboratories, West Chester, Pennsylvania

In the 1950's this plant was a major manufacturer of penicillin. Factory wastes of spent fermentation broths and sanitary sewage were combined with the town's wastes and sent to a newly constructed trickling filter plant under auspices of the town. Problems soon developed, and Wyeth Labs initiated pilot studies to determine if their wastes could be treated by the "complete-mixing" activated sludge process before discharge to the municipal sewer.

The fermentation broths were made up of corn steep liquor, lactose and mineral salts. After appropriate fermentation, the fungi mycelium was separated from the spent broth by vacuum filtration. The penicillin was extracted from the broth with a solvent such as amyl acetate in an acid solution. After retrieving the penicillin, the solvent was recovered by stripping for further reuse. The remaining spent fermentation broth had an extremely high BOD concentration and low pH. Separate disposal of the mycelium filter cake served to produce a fermentation wastewater quite low in TSS, if not in soluble organic matter.

The Company studies focused on treatment and disposal of spent fermentation broths and culminated in the construction of full-scale pretreatment facilities during 1957-58. The full-scale Wyeth treatment installation was designed to handle spent fermentation broths and domestic sewage, amounting to 850 m^3/day (225,000 gpd) at pH 2.0 and with COD waste strength of 2,560 mg/l equivalent to 2,176 kg (4,800 lb) COD/day. No primary settling was employed. Prior to entering the aeration tanks, the wastes were to be neutralized with caustic to a pH of about 6.5. Two aeration basins were constructed in parallel each of 1,160 m^3 (41,000 ft^3) capacity. The tanks were based on removal of 0.96 kg COD/m^3 (60 lbs/1,000 ft^3)/day. It was estimated that 3 kg (7 lb) of sludge would be generated for each 45 kg (100 lb) COD removed. The wastes then entered two final clarifiers operating in parallel designed to give a hydraulic overflow rate of 6.5 m^3/day/m^2 (160 gpd/ft^2) and a waste detention time of 7 hr. No sludge digestion facilities were built, since excess sludges would be sent to the municipal treatment plant. The treated effluent was expected to contain less than 50 mg/l soluble BOD and 180 to 260 mg/l volatile suspended solids (36, 50).

Initially, only spent fermentation broths were sent to the treatment plant. Data collected Aug. 1958 to Feb. 1959 showed an average waste flow into treatment of only 113 m^3/day (30,000 gpd), containing about 1,130 kg (2,500 lb) COD/day. The average COD in the raw waste was 9,750 mg/l but COD strengths varied widely from 2,400 mg/l to over 30,000 mg/l. Data subsequently collected during Feb. and Mar. 1959 showed an average raw waste flow of 132 m^3/day (35,000 gpd) commensurate with an average COD strength of 17,300 mg/l, thereby giving a daily COD loading about 2,290 kg (5,050 lb)/day. The latter loading appeared to exceed the design level of the treatment plant. The treatment of spent broths by themselves resulted in an extremely strong waste with very long treatment retention time (about 23 days). The effluent COD's stabilized around 880 mg/l, indicative mostly of non-biologically oxidizable materials remaining.

During the first year of pretreatment, very high effluent TSS values were traced to the waste neutralization practices and excessive buildup of inert organic solids in the aeration basin. Process changes were instituted to minimize these problems. Nitrogen content, TSS and pH levels were found somewhat interdependent. Ample nitrogen in the spent fermentation broths provided the opportunity of delivering an effluent at almost any stage of nitrification. When approaching nitrification, periods of low flows tend to throw the plant into denitrification and bulking sludge. Incoming raw wastes were adjusted to pH 6.5 by soda ash before entering the aeration basin. Biological oxidation resulted in the release of ammonium ions which kept the pH level above 6.5. Conversion of ammonium to nitrates and nitrites with excess aeration caused a loss in the ammonium carbonate buffering capacity of the system leading to lower pH's, greater potential for filamentous growths, and eventually a poor-settling sludge. Careful control of the pH level chemically was therefore necessary. If operations were conducted almost entirely within the ammonia range, slight overloads or reductions in oxygen transfer could also result in undue Sphaerotilis growths and sludge bulking (36, 50).

An increase in fine chemicals production was experienced at the Wyeth plant around 1959-60. This not only greatly increased COD loads but also changed the character of the combined wastes from acid to alkaline. The wastewaters furthermore became heavily saturated with inorganic salts. Preliminary estimates in 1960 indicated that total COD loads would approximate 2,720 kg (6,000 lb)/day, and hydraulic loads could be about 378 to 568 m^3/day (100,000 to 150,000 gpd). Pilot plant studies were resumed by the Company to determine impact upon the pretreatment works.

With the introduction of the fine chemical wastes in the early 1960's, aerator loads were about 1.2 kg COD/day/m^3 (73 lb COD/day/1,000 ft^3) aerator volume. Predictions were made for 4.5 kg (10 lb) sludge to be produced for each 45 kg (100 lb) COD removed, an effluent COD of 600 mg/l from the pretreatment facilities and a 90 percent BOD removal efficiency. An equalizing tank was added to achieve full blending of acid and alkaline wastes. After collecting only one month of data, peaks as high as 4,500 kg (10,000 lb COD)/day were recorded. An average daily hydraulic load of 500 m^3/day (138,800 gpd) was also measured (50).

It was reported in 1963(4) that studies were conducted on a waste mixture that contained 60 percent combined plant sewage plus 20 percent each of the waste broth and fine chemical waste, the latter two amounting to 76 m^3/day (20,000 gpd) each. Blending of the alkaline and acid wastes followed by pH adjustment to 7.0 with sulfuric acid gave an incidental 30 to 35 percent COD reduction. After neutralization and equalization, the waste mixture was subjected to complete-mixing activated sludge. COD removal in a series of eight pilot runs varied from 81.5 to 95.0 percent, averaging 90 percent. With proper modifications, the pretreatment facilities could successfully cope with the new fine chemical wastes. The system consistently showed 90 percent BOD removal and up to 90 percent COD removal. Industrial pretreatment followed by municipal treatment were thought capable of providing overall BOD removals of 97 to 98 percent for the Wyeth Laboratories' wastes.

Fermentation and Biologicals

Lederle Laboratories, Pearl River, New York

Lederle Laboratories is a major manufacturer of antibiotics. Main processing consists of fermentation, although synthesized organic chemicals such as vitamins are also produced. Biologicals produced include vaccines and antitoxins (12, 24, 44, 119).

In the plant, spent fermentation beers are generally recovered in wet form. Some may be dried and sold as animal feed supplements, but most is taken to landfill or spread onto nearby farmlands. Bad fermentation batches usually go to the waste treatment plant.

Molof (12) reviewed 15 years of waste treatment acitivity at Lederle. The treated industrial effluents are transported by gravity to the Orangetown, N.Y. municipal trickling filter treatment plant wherein municipal and industrial waste streams are mixed roughly in a ratio of 1:1. The final municipal effluent is released to the Hackensack River Basin, an important watershed for domestic water supply.

In the early 1960's Lederle had a two-stage trickling filter plant. In 1961 the Company completed the conversion of existing tanks into an activated sludge plant serving in tandem with the dual-stage trickling filter system. The activated sludge system consisted of an aeration tank divided into four compartments with a total capacity of 830 m^3 (220,000 gal) which was followed by a secondary clarifier and a storage tank of 757 m^3 (200,000 gal). Clarifier sludges could be returned to the activated sludge chamber.

Although wastes were settled before entering the trickling filters, there were no provisions for settling prior to activated sludge treatment. The two biological processes were linked by a flow division box. Three separate flows entered the division box, one having relatively low BOD, a second with medium BOD, and the third with high BOD. The division box thus controlled the BOD loading to each biological process. The activated sludge process was designed for a hydraulic load of 1,890 m^3/day (0.5 mgd), or about half of the total wastewater flows being treated. Another link between the two processes resulted from the storage during the daytime hours of the activated sludge effluents in a 757 m^3 (200,000 gal) tank. At night, this liquid was sent either to the trickling filter plant or to the municipal sewers. This storage was necessary due to limits on maximum flows that could be accepted by the municipality during the daytime.

Special pretreatment provisions were made for wastes from the solvent recovery sector, the mash filtrates, and discarded fermenter mashes. Empty tanks were used for the separate aeration of collected and stored wastes. The most concentrated waste streams generally resulted from solvent recovery. A selected solvent may have a BOD of about 2 million mg/l or 1.6 kg BOD/l (13 lb BOD/gal). This solvent is some 6,250 times stronger than sanitary sewage in BOD strength. Therefore, variations at the solvent recovery unit can create wide variance in the raw waste loadings. These pretreatment operations at Lederle were said to significantly absorb surges in both organic and hydraulic loadings.

Operational data were somewhat sparse at the time of the 1962 status report because the activated sludge process had been in operation only eight months. The activated sludge system was receiving, with no odor problem, about 1.9 kg/m^3 (120 lb/1,000 ft^3) BOD/day. The trickling filter system was receiving about 1.4 kg/m^3 (90 lb/1,000 ft^3) BOD/day with definite odor characteristics. The activated sludge process also tended to produce a clearer effluent. Disadvantages of the activated sludge process were that it required more technical control than the filters and its lesser ability to handle shock loads (12).

After two years of study and in large part due to severe odor problems, the Company selected the *Unox Pure Oxygen Aeration Process*, and this unique activated sludge system was finally completed full-scale in March 1972. This new system, at a reported cost of $2.5 to $3.0 million replaced all previous systems. The Unox system was designed to treat an average flow of 5,680 m^3/day (1.5 mgd) with hourly peaks up to 11,400 m^3/day (3.0 mgd). The average organic load of the treatment facility was designed at 18,100 kg (40,000 lb) BOD/day with acceptable peak loads up to 29,500 kg (65,000 lb) BOD/day. The treatment works expects to produce an effluent with less than 250 mg/l BOD and 250 mg/l TSS.

The main treatment unit is the closed reactor, a multichambered aeration tank fitted with a gas-tight precast concrete lid. A typical reactor has three separate chambers or stages, separated by baffles, with tank depths from 3 m (10 ft) up to 9 m (30 ft). The Lederle reactor has a 3,100 m^3 (820,000 gal) capacity with a dual train, a total of six bays.

Oxygen is supplied to the aeration tank on demand. When oxygen pressure decreases in the reactor, a flow controller is activated permitting more oxygen to enter. Oxygen is produced on site by a molecular sieve generator.

Mechanical surface aerators bring the pure oxygen into solution. Liquids and oxygen are introduced into the first chamber, the oxygen filling the space between the liquid level and the tank lid. An agitator then whips up the wastewater to contact the oxygen. The reactor has a normal liquid depth of 3 to 3.6 m (10 to 12 ft) with a 1.2 m (4 ft) blanket of pure oxygen above. Oxygen and wastewater pass concurrently through each successive contacting stage, and the effluents from the last stage leave the Unox chamber, for settling in conventional clarifiers.

The Unox unit provides an oxygen dissolution capacity of 12,200 kg (27,000 lb) oxygen/day at a 90 percent utilization efficiency. The reactor effluents are calculated to contain a minimum of 5 mg/l dissolved oxygen. Activated sludge is recycled to the head end of the pure oxygen reactor. A return sludge to incoming sewage flow ratio of about 1:1 is maintained. The last pure oxygen contact stage is provided with means of venting exhaust gases.

Other treatment units at Lederle include a flash mixer and a clariflocculator, 18 m (60 ft) in diameter, preceding the Unox process. Following the activated sludge process, there are three 12 m (40 ft) diameter clarifiers arranged in parallel, plus chlorination of final effluents. Since the Unox system utilizes pure oxygen, a combustible gas analyzer and a TOC analyzer were installed on the effluents from the clariflocculator to warn of dangerous elements such as solvents and explosive gases in the system. Given certain conditions, the oxygen delivery is shut off and/or the wastewaters can be diverted around the reactor. In the event the exhaust gases from the reactor may create odors, ozonation provisions have been made available. A series of cooling towers are utilized for significant reuse of cooling water, principally in fermentation. The COD:BOD ratio of incoming raw feed into treatment approximates 1.4 and that of the outflows averages 2.0. The latter ratio is surprisingly low.

Before entering treatment, the raw process pharmaceutical wastes contain from 9,070 to 11,300 kg (20,000 to 25,000 lb) BOD/day and 4,540 kg (10,000 lb) TSS/day or more. In June 1972, the Company verbally reported an average BOD entering the industrial waste treatment system of 9,800 kg (21,600 lb)/day with outflows approximating 975 kg (2,150 lb)/day (about 90 percent BOD removal prior to municipal "secondary" treatment). Primary and secondary sludges from the treatment plant are vacuum filtered. The dewatered biological sludges may be mixed with straw and sawdust and composted; otherwise, these materials are incinerated or taken to landfill for ultimate disposal (12, 24, 44, 119).

Drug Formulation

Dorsey Laboratories, Lincoln, Nebraska

Anderson, et al. (2, 38) conducted detailed studies in 1968-69 of the characteristics and treatability of wastewaters from the Dorsey Laboratories' pharmaceuticals formulation plant at Lincoln, Nebr. Attempts were made to correct serious deficiencies in the existing extended aeration treatment facilities. Correction procedures were, however, deemed largely impractical and future plans called for connection to the city of Lincoln municipal sewerage following industrial pretreatment. The Laboratories employ 225 people during a single-shift, 40-hr, 5-day work week. The plant conducts batch processing and the product mix changes frequently. Products are primarily of the non-prescriptive type either liquid or tablet form. These include sedatives, digestive aids and various medications for arthritis, coughs, colds, hay fever, sinus and bacterial infections.

Wastewaters to the extended aeration treatment facilities included sanitary and cafeteria wastes and spent waters from production and cleanup operations. Spent cooling waters and boiler blowdowns were excluded from the treatment system. The aeration basin and settling chamber were 79.5 m^3 (21,000 gal) and 7.3 m^3 (1,935 gal) respectively. Design retention time in the aeration basin was 25 hr, and the design organic load (inflow) was 30.8 kg (68 lb) BOD/day. There were no provisions for wasting excess sludge or sludge recycle. Furthermore, there was no equalization of the raw waste flows occurring over the 8 to 10 hr process cycle each day, or of the high hourly variation in waste strength.

Since 1965, the extended aeration plant had experienced serious operational problems such as bulking sludge, excessive loss of biological solids from the system, and overload conditions. Resulting effluents were far from satisfactory.

The studies by Anderson et al. were divided into three phases:

1. Initial evaluation of the existing treatment system and nature of wastewaters;
2. Treatability of the wastes in a laboratory-scale treatment system;
3. Incorporation of findings into a detailed appraisal of the existing treatment plant.

During the first phase, daily composites were taken of the influent and effluent (Table VIII-3). TSS and VSS in the effluents were much higher than the levels entering the plant. Also, BOD reductions were only in the 30 to 70 percent range.

During the second phase, the laboratory extended aeration treatment system was operated continuously for 114 days. The laboratory tests indicated that the wastewaters coming from the Dorsey Laboratories contained relatively high concentrations of mono- and di-saccharides, determined to be quite conducive to filamentous growths of Sphaerotilis natans. Sphaerotilis is a leading cause of sludge bulking, and it was reported as one of the major contributing factors to the operational problems encountered in the existing treatment plant. Nitrogen determinations made on the raw wastewaters suggested a possible nitrogen deficiency. Difficulties were experienced in performance of the laboratory system and the system was reported to have failed at least twice.

In the third phase, operational modifications were made to the treatment plant and there was additional daily composite sampling and evaluation from May 26 to Sept. 30, 1969 (Table VIII-4). Again, the influent flows varied greatly over the recording period. On the 18th day of the study, high strength sugar wastes started to enter the system from the manufacturing of cough syrup, and Sphaerotilis forms promptly increased. To preclude system failure, the Company consented to keeping the strong sugar waste out of the circuit from the 42nd to the 72nd day of the survey. Nevertheless, operational problems were still evident. About the 73rd day, discharge of the sugar wastes resumed, and in spite of a daily application of 5.4 to 6.8 kg (12 to 15 lb) ammonium phosphate to the basin, S. natans growths were increasing. Measurements were not made from the 87th until about the 121st day of operation.

Results of grab samples collected on Sept. 21 showed that MLSS concentrations had dropped from previous levels of 2,000 and 3,500 mg/l to much less than 1,000 mg/l, and dispersed growths were highly prevalent. Discussions with Company personnel also revealed during this latter period that sulfa drugs had been produced at the factory. Over the last few days of study culminating on Sept. 30, 1969, the system demonstrated partial recovery with a MLSS level of 2,400 mg/l reached on Sept. 30. Besides wide hourly variations in waste strengths and flows, odors, ozonation provisions have been made available. A series of cooling towers are utilized for significant reuse of cooling water, principally in fermentation. The COD:BOD ratio of incoming raw feed into treatment approximates 1.4 and that of the outflows averages 2.0. The latter ratio is surprisingly low.

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Dorsey Laboratories, Lincoln, Nebraska

Anderson, et al. (2, 38) conducted detailed studies in 1968-69 of the characteristics and treatability of wastewaters from the Dorsey Laboratories' pharmaceuticals formulation plant at Lincoln, Nebr. Attempts were made to correct serious deficiencies in the existing extended aeration treatment facilities. Correction procedures were, however, deemed largely impractical and future plans called for connection to the city of Lincoln municipal sewerage following industrial pretreatment. The Laboratories employ 225 people during a single-shift, 40-hr, 5-day work week. The plant conducts batch processing and the product mix changes frequently. Products are primarily of the nonprescriptive type either liquid or tablet form. These include sedatives, digestive aids and various medications for arthritis, coughs, colds, hay fever, sinus and bacterial infections.

Wastewaters to the extended aeration treatment facilities included sanitary and cafeteria wastes and spent waters from production and cleanup operations. Spent cooling waters and boiler blowdowns were excluded from the treatment system. The aeration basin and settling chamber were 79.5 m^3 (21,000 gal) and 7.3 m^3 (1,935 gal) respectively. Design retention time in the aeration basin was 25 hr, and the design organic load (inflow) was 30.8 kg (68 lb) BOD/day. There were no provisions for wasting excess sludge or sludge recycle. Furthermore, there was no equalization of the raw waste flows occurring over the 8 to 10 hr process cycle each day, or of the high hourly variation in waste strength.

Since 1965, the extended aeration plant had experienced serious operational problems such as bulking sludge, excessive loss of biological solids from the system, and overload conditions. Resulting effluents were far from satisfactory.

The studies by Anderson et al. were divided into three phases:

1. Initial evaluation of the existing treatment system and nature of wastewaters;
2. Treatability of the wastes in a laboratory-scale treatment system;
3. Incorporation of findings into a detailed appraisal of the existing treatment plant.

During the first phase, daily composites were taken of the influent and effluent (Table VIII-3). TSS and VSS in the effluents were much higher than the levels entering the plant. Also, BOD reductions were only in the 30 to 70 percent range.

During the second phase, the laboratory extended aeration treatment system was operated continuously for 114 days. The laboratory tests indicated that the wastewaters coming from the Dorsey Laboratories contained relatively high concentrations of mono- and di-saccharides, determined to be quite conducive to filamentous growths of Sphaerotilis natans. Sphaerotilis is a leading cause of sludge bulking, and it was reported as one of the major contributing factors to the operational problems encountered in the existing treatment plant. Nitrogen determinations made on the raw wastewaters suggested a possible nitrogen deficiency. Difficulties were experienced in performance of the laboratory system and the system was reported to have failed at least twice.

In the third phase, operational modifications were made to the treatment plant and there was additional daily composite sampling and evaluation from May 26 to Sept. 30, 1969 (Table VIII-4). Again, the influent flows varied greatly over the recording period. On the 18th day of the study, high strength sugar wastes started to enter the system from the manufacturing of cough syrup, and Sphaerotilis forms promptly increased. To preclude system failure, the Company consented to keeping the strong sugar waste out of the circuit from the 42nd to the 72nd day of the survey. Nevertheless, operational problems were still evident. About the 73rd day, discharge of the sugar wastes resumed, and in spite of a daily application of 5.4 to 6.8 kg (12 to 15 lb) ammonium phosphate to the basin, S. natans growths were increasing. Measurements were not made from the 87th until about the 121st day of operation.

Results of grab samples collected on Sept. 21 showed that MLSS concentrations had dropped from previous levels of 2,000 and 3,500 mg/l to much less than 1,000 mg/l, and dispersed growths were highly prevalent. Discussions with Company personnel also revealed during this latter period that sulfa drugs had been produced at the factory. Over the last few days of study culminating on Sept. 30, 1969, the system demonstrated partial recovery with a MLSS level of 2,400 mg/l reached on Sept. 30. Besides wide hourly variations in waste strengths and flows,

Table VIII-3

Waste Treatment Performance Data, Phase 1
Dorsey Labs, Lincoln, Nebr.

Parameters	Sample Dates, 1968					
	Jan. 3		Feb. 13		Mar. 19	
	(m^3/day)	(gpd)	(m^3/day)	(gpd)	(m^3/day)	(gpd)
Avg. flow	23.5	6,200	20	5,400	58	15,400
Max. flow	110	29,000	107	28,300	173	45,600
Detention time, days		3.4		3.9		1.4
	(mg/l)					
BOD influent		820		1,140		840
BOD effluent		570		350		250
BOD % removal		30		69		70
COD influent		1,520		2,770		1,960
TVS influent		832		1,510		486
TVS effluent		900		785		365
TSS influent		218		249		81
TSS effluent		688		630		250
VSS influent		147		199		72
VSS effluent		646		532		241
VSS % removal		0		0		0
	kg/day	(lb/day)				
BOD influent	19	(42.4)	23	(51.4)	49	(108.0)

Table VIII-4

Waste Treatment Performance Data, Phase 3
Dorsey Labs, Lincoln, Nebr.

Parameters	Composite Sample Dates, 1969							
	6/12	6/25	7/15[a]	7/31[a]	8/6[a]	8/14	8/21	9/30
Cumulative Days of Study	17	30	50	66	72	80	87	127
Avg. Flow:								
m^3/day	15	20	35	68	72	23	98	18
(gpd)	(4,000)	(5,200)	(9,300)	(18,000)	(18,900)	(6,000)	(25,900)	(4,800)
Max. Flow:								
m^3/day	38	40	83	23	360	102	235	8
(gpd)	(10,000)	(10,500)	(22,000)	(61,000)	(95,000)	(27,000)	(62,000)	(21,500)
	(mg/1)							
BOD effluent	3	9	-	30	-	50	-	475
COD influent	375	375	540	410	680	3,210	660	3,580
COD effluent	50	30	90	110	-	210	-	1,340
COD, % removal	87	92	83	73	-	93	-	63
TVS influent	279	264	178	156	364	2,240	544	1,770
VSS influent	80	140	48	48	131	203	77	129
VSS effluent	97	155	42	98	261	105	36	400
VSS, % removal	0	0	13	0	0	48	53	0

[a] High-strength sugar wastes being bypassed around treatment plant on or about these dates. Results for these dates presumably reflect treatment performance *only* for the raw wastes actually reaching and passing through treatment system.

hydraulic loads to the treatment plant on certain days were in excess of 450 percent of the design criteria. Organic loads frequently appeared to be at least 50 percent higher than design specifications. The study concluded:

1. The existing aeration system was incapable of providing a high level of treatment for this waste.
2. BOD determinations were complicated not only by variability in amounts and character of the wastes but also by the presence of inhibiting substances.
3. Abundant growths of S. natans leading to bulking sludge, was one of the primary reasons for continued failure of the system.
4. **Many operational problems were prevailing within the system.**
5. Even though problems were identified, the investigators could see no practical solutions possible, other than costly pretreatment and piping modifications.

TRICKLING FILTRATION

Fermentation

The Upjohn Company, Kalamazoo, Michigan

Tompkins (17) reviewed performance of the trickling filter treatment plant at the Upjohn pharmaceuticals plant from 1948 through 1956. The facilities were primarily receiving antibiotics fermentation wastes, but also sanitary wastes. A balance was attempted between the amount of spent fermentation beers that could be accepted into the treatment works vs that which were necessarily hauled to field disposal. Edmondson (60) indicated the possibility that substances in the antibiotic spent beers would depress and/or be toxic to biological growths on the trickling filters.

The fermentation processes increased rapidly in the early 1950's. The trickling filter plant was stressed under heavy loads at that time, and, in spite of significant expansion of the biological treatment facilities in 1953, hauling of spent fermentation beers had to be continued.

The treatment plant discharged to a small trout stream. Plant effluent was limited by the State to 45 kg (100 lb) BOD/day, which was significantly exceeded through most of 1951-1952. The effluent was also subject to chlorination provisions from May 15 to Sept. 15, yielding a 0.5 mg/l minimum residual (17).

The original plant had a maximum capacity of 2,650 m^3/day (700,000 gpd) with two 27 m (90 ft) diameter filters, operated both in parallel and series, with a pair of primary settlers and a pair of final settlers. The spent beers, before entering the main treatment plant, were held in two pre-aeration tanks, each 95 m^3 (25,000 gal).

An antibiotic introduced in the spring of 1952 created a spent beer of 20,000 to 30,000 mg/l BOD, whereas previous beers were about 5,000 mg/l. This caused a serious treatment plant overload. Hauling spent beers to land disposal was greatly increased, and these wastes were heavily chlorinated. At times, the effluent of the treatment plant was almost as high as the influent in TSS (17).

Treatment plant expansion in spring 1953 added an additional primary settler, converted the pair of final settlers to intermediate clarifiers, added two final sedimentation basins, a new 37 m (120 ft) diameter filter, and increased pumping capacity. Improvements were also made on the fermentation beer pre-aeration tanks, and a grit chamber was added. Even though the spent beers had a pH range of 2 to 11, when mixed with large volumes of washwaters the pH extremes were minimized and pH adjustment was unnecessary.

In spite of doubling the design capacity of the anaerobic sludge digester, problems with solids existed from 1948 onward. There were breaks in the digester waste gas line, and a poor supernatant quality from the digester was attributed to greasy sludges entering the digester, thereby decreasing the solids settling ability. Grease or lard oil used as a defoamer in the antibiotics production decreased trickling filter performance and caused shock loads. The oils remained emulsified, causing solids buildup and ponding on the filters and significantly hampered BOD reductions. The use of Daphnia demonstrated the presence of toxic wastes.

Since 1953, BOD reductions have been 95 to 98 percent. At an average flow rate of 2,300 m^3/day (600,000 gpd) and 1,200 kg (3,080 lb) BOD/day to the treatment plant, final effluents contained an average of 41 kg (90 lb) BOD/day. Average influent and effluent BOD strengths were respectively 600 mg/l and 20 mg/l. During the warm months, the unchlorinated final effluents amounting to 380 m^3/day (100,000 gpd) were used for irrigation of lawns around the plant. Besides other benefits, chlorine consumption was reduced significantly. Nevertheless, it was reported that hauling of excess spent antibiotic beers was still continuing through the mid-1950's (17).

Great Britain Plants

In the mid-1960's, biological trickling filters used on mixed wastes (from fermentation, and other industries) showed that the filters may be loaded at about 0.6 kg/m^3 (1 lb/yd^3) BOD/day to achieve about 96 percent removal. High-rate filters in series, with and without recirculation, have been successfully used with loads up to 1 kg/m^3

(2 lb/yd^3 BOD)/day on the first stage. Resulting sludges are digested with the production of fuel gas, and the digested sludges are dried, incinerated and/or disposed of by land spreading or landfill.

Biological filtration was apparently preferred in Great Britain to the activated sludge process. It was inferred that trickling filtration may be somewhat less susceptible to shock waste loads, or become colonized by micro-organisms more resistant to the antibiotic residues contained in the wastes.

Fermentation/Synthesized Organic Chemicals

The Upjohn Company, Kalamazoo, Michigan

In view of rapidly increasing production in the 1950's, the Upjohn pharmaceuticals plant evaluated many forms of waste treatment for technical and economic feasibility. Cushman and Hayes (57) reported in 1956 on pilot plant trickling filtration studies using various combinations of fermentation, synthesized organic chemical and sanitary wastewaters from Upjohn. Paradiso in 1955 (68) noted that due to the high volumes and high BOD of the fine chemical wastes that the cost for biological facilities would exceed $2 million and were therefore not feasible. Deep well disposal installed in 1952 also temporarily minimized the need for additional treatment of the chemical wastes. Nevertheless, Paradiso maintained these wastes would be amenable to biological oxidation, and from the data obtained either two-stage trickling filtration or two-stage activated sludge could give 95 percent reduction of the BOD loads.

The types of wastewaters received into the trickling filter pilot plant included:

1. Synthesized organic chemical waste in the BOD range of 2,000 to 10,000 mg/l, chiefly consisting of spent mineral acids and their salts, alcohols, chlorinated and unchlorinated hydrocarbons, organic acids, aldehydes, ketones, and residual fractions of heterocyclic steroids and their intermediates.

2. Sanitary wastes plus miscellaneous industrial wastes from the fine chemicals and antibiotic sectors, including varying amounts of spillage products, tank washings, breakage, filter cake, organic solvents, oils, greases and some fermentation byproducts. This stream had a BOD strength of 200 to 1,400 mg/l.

3. Spent antibiotic fermentation broth with a BOD range of 3,000 to 15,000 mg/l (57).

Each waste blend was neutralized into the pH range of 6.5 to 7.0. Trickling filter units were used in a two-stage setup with primary settling, intermediate settling between the two filters, and final settling following the second filter. Pre-aeration of the feed tank to the pilot plant was employed for four of the seven waste blends. Influents and effluents from the pilot plant were tested for antibacterial activity using B. subtilis (neomycin test organism) and M. aureus ATTC 9114 (erythromycin test organism).

The test results showed that the spent fermentation beers generally contained ample nutrients for proper biological growths, and no supplement was necessary. However, the beer content had to be maintained below 30 percent by volume in the total waste mixtures. With the various mixtures of chemical, sanitary and fermentation wastes, the incoming BOD levels ranged between 550 and 4,080 mg/l, and BOD reductions were 93.9 to 99.5 percent. Effluent BOD values were generally below 30 mg/l except for the chemical-sanitary waste blend, which was much higher. Influent nitrogen levels were in the range of 18 to 168 mg/l. Corresponding nitrogen reductions for the various blends of wastes through the two-stage trickling filter system were between 55.7 and 95.4 percent, but generally in excess of 80 percent. The pilot plant was operated 18 months.

The study report concluded that all wastes investigated were treated by biological filtration to a high degree (57).

American Cyanamid, Willow Island, W. Virginia

Fine chemicals and antibiotics waste treatment at the American Cyanamid plant in the early 1950's was described in a series of three papers by Vogler, Brown and Griffin (18). Vogler outlined the treatment system utilized for chemical wastewaters in 1950-51; Brown described the expected characteristics of the new antibiotic aureomycin wastes; and Griffin gave design details on the additional treatment facilities necessary for the fermentation liquors.

Synthesized organic chemicals production included the manufacturing of melamine (used for melamine-urea and melamine-formaldehyde resins); various pigments such as iron blue, chrome yellow, chrome green, and molybdate orange; various brighteners; folic acid (which can be used as a vitamin); and a host of pharmaceutical intermediates.

The early treatment system was an earthen holding basin with a surface area of 3.6 hectares (7.2 acres) and a capacity of 27.5 mg. This system received sanitary, cafeteria, power plant and manufacturing effluents, and the storm waters collected over the plant property. At an average wastewater flow of 12,700 m^3/day (3.4 mgd), the lagoon was providing about 8 days' waste detention. Final discharge was made to Cow Creek, a small tributary which flowed about 0.8 km (0.5 mi) to the Ohio River.

Raw manufacturing wastewaters from the plant largely consisted of spent mother liquors, filtrates, column slops, washing and cooling waters. Principal pollutants were organic byproducts, acids, alkalies and salts. Total waste flow reported as 12,700 m^3/day (3.4 mgd) in 1950 was subsequently reduced to 9,400 m^3/day (2.5 mgd) by in-plant water conservation measures. Raw wastes had high color and ranged in BOD from 46 to 150 mg/l, averaging 80 mg/l; pH varied from 2.5 to 8.0, averaging 5.9; and TS and TSS approximated 1,500 mg/l and 200 mg/l, respectively. The lagoon effluents were pale green with average values of 33 mg/l BOD, a pH of 7.6, and TS and TSS of 1,300 mg/l and 100 mg/l, respectively. The lagoon influent loading was about 1,000 kg (2,300 lb) BOD daily equivalent to 12 kg (27 lb)/acre-foot of lagoon capacity/day. Average BOD and TSS reductions were about 50 percent.

In 1950, the decision was made to manufacture the antibiotic aureomycin at the Willow Island plant. Aureomycin (chlorotetracycline) was one of the first broad spectrum antibiotics available in the pharmaceutical industry.

Aureomycin wastes were divided according to source as follows:

1. Strong fermentation beers and filtrates of high BOD, ranging from 4,000 to 7,000 mg/l. Aureomycin was fermented in a medium of sugars, corn steep liquors and nutrient salts. After separation of mycelium, the fermentation broth is passed through layers of Magnesol which absorb the desired chemical values. Absorption of B_{12}, a growth-producing vitamin, from the fermentation broth was cited. The relationship of vitamin B_{12} to aureomycin was not precisely defined. Spent filtrates and washes were reported discharged to the sewer, a source of high BOD wastes.

2. Washings of equipment and plant floors ranging in BOD from 600 to 1,500 mg/l

3. Inorganic solids including filter cakes and precoat from the vacuum filters. Precoat (Filter-Cel) and diatamaceous earth, serving as filter aids, both enter the sewer.

4. Chemical wastes, including spills of acids and alkalies, and spent butanol and brines, resulting from refining of the drugs. Most butanol was reported as recovered and reused, but a significant quantity was lost as wastage and/or contained within the residual "heels" remaining after distillation. Butanol has an extremely high BOD content, i.e.~0.68 kg (~1.5 lb) BOD for each kg (lb) of butanol lost. The heels may contain up to 500,000 mg/l BOD and the total sewered load from this source alone may amount to 1,400 kg (3,000 lb) BOD daily. Associated spent brines may total 54 metric tons (60 tons)/day, expressed as the dry salt.

Full fermentation production was expected to generate an average of 600 m^3/day (160,000 gpd) wastewaters containing 3,600 kg (8,000 lb) BOD daily. At this flow, BOD raw waste strength was calculated as 6,000 mg/l. Because fermenters occasionally run wild and may be suddenly dumped, the treatment plant was designed for 2,400 m^3/day (450 gpm) with a hydraulic maximum of 3,300 m^3/day (600 gpm). Mycelium and diatamaceous earth removed by filtering of the spent fermentation beers were estimated as amounting to 1,100 m^3 (600 ft^3/day) sludges at 8 to 10 percent solids, requiring satisfactory disposal.

Based on previous Company experience, trickling filtration was selected as the prime means of treating the Willow Island fermentation wastes. Solvents mixed with salts from the refining end of the antibiotics process were judged adverse to biological treatment, and it was therefore planned to sewer these streams into the existing chemical waste treatment lagoon. These streams were estimated to contribute 390 kg (900 lb) BOD/day to the 390 kg/day already in the lagoon. The objective of 100 mg/l BOD in the combined effluent flows of 19,500 m^3/day (5.16 mgd) gave a total plant allowable BOD load of 2,000 kg (4,300 lb)/day, thereby leaving 1,100 kg (2,500 lb)/day of BOD as a maximum coming from the fermentation treatment works. The TSS effluent objective was 80 mg/l. The trickling filtration plant had to be designed for an average BOD removal of 68.8 percent, which was not overly demanding.

The sequence of treatment steps to properly handle the antibiotic waste would comprise pH control by adding lime to the entering wastes; pre-aeration and 12-hr wastewater holding within an equalization basin; parallel 5 m (16 ft) diameter primary clarifiers; parallel 24 m (80 ft) diameter high-rate biofilters; and parallel 5 m (16 ft) diameter secondary clarifiers.

Secondary sludges would be returned ahead of the primary clarifiers, and sludges removed from the primary settlers were to be pumped and dewatered on a 2 x 2 m (6 x 6 ft) vacuum filter. Lime and ferric chloride were to be added to the sludges to aid in dewatering. Filtrates from the vacuum filter would be returned to the pH control box. The trickling filters were designed for an average recirculation ratio of 3 volumes of filter effluent to 1 volume of raw wastes passing onto the filters. Dewatered sludges were to be disposed of to landfill.

The final Willow Island plant effluents representing the combined treated antibiotic and chemical waste flows would receive full chlorination before ultimate discharge to Cow Creek and the Ohio River (18).

Fermentation and Biologicals

Lederle Laboratories, Pearl River, New York

Since the end of World War II, the Pearl River plant has produced antibiotics (penicillin and aureomycin), vitamin B_{12} and biologicals. Brown classified the waste streams from Lederle (18, 101) as follows:

1. Strong fermentation beers with BOD's from 4,000 to 8,000 mg/l

2. Inorganic solids, including precoat and filter aid used in filtering out mycelium

3. Washings of floor and equipment contributing a large part of the hydraulic load and containing from 600 to 2,500 mg/l BOD

4. Chemical wastes containing spent or lost acids, alkalis, salts and solvents. A pound of solvent lost, such as acetone or butanol, can exert 0.5 to 0.7 kg (1 to 1.5 lb) of BOD. Salt loads can amount to many tons per day found in the waste streams.

5. Barometric condenser waters resulting from the evaporation and drying processes. These waters usually are of extremely large volume and therefore are not generally discharged through the treatment plant. The BOD of these waters can range from 60 to 120 mg/l; these loads can be high.

Solid wastes from the Laboratories including infected manures, glassware, filter cakes, cafeteria and miscellaneous trash, were sent to a double-hearth incinerator. Sewage sludge, previously dried to about 70 percent moisture, was also received into this incinerator. Through the late 1940's, spent penicillin fermentation broth was being evaporated to give a slurry with about 10 to 15 percent solids. This was then spray dried to produce an animal feed supplement. However, the aureomycin spent broth when spray dried was found to carmelize, making the procedure impractical. Excluding weak sewage, the main process waste stream from Lederle was about 1,600 m^3/day (0.425 mgd) with 2,500 mg/l to 3,000 mg/l BOD. The raw waste equivalent was estimated in the order of 3,600 to 4,500 kg (8,000 to 10,000 lb) BOD/day.

Following pilot plant studies for a high-rate trickling filter treatment plant, the first 31 m (100 ft) filter was completed in July 1949, the second in July 1950 and the third in 1952. These filters operated in parallel following three 12 m (40 ft) diameter parallel primary clarifiers. A tank providing plain aeration and 4 to 4.5 hr waste detention was installed ahead of the primary clarifiers in the fall of 1950. The remainder of the treatment plant, apparently completed during 1951, consisted of a storage tank for partial equalization of raw wastes from the manufacturing sectors, followed by pH adjustment, and grease removal by flotation. These units preceded the 4.5 hr aeration tank, the primary clarifiers and the three large trickling filters. A 12 m (40 ft) diameter (single) secondary clarifier was added in the early 1950's, together with chlorination facilities for disinfection of final effluents. The treated industrial effluents from Lederle were subsequently delivered to the local municipality for further biological treatment.

Waste studies on the treatment plant showed BOD removal through the tank providing plain aeration was about 30 percent, with the influent and effluent averaging 2,500 and 1,750 mg/l, respectively, in December 1950. Raw waste TSS was in the range of 1,000 to 1,200 mg/l, but 60 percent of the solids were nonvolatile. This high ash content was due to diatamaceous earth and filter aid lost from mycelium separation. The primary and secondary sludges, after dewatering via vacuum filtration, at times reached 9 to 12 percent solids with an ash content as high as 70 percent, again due to abnormally high loss of fermentation filtered materials. Although the diatamaceous earth entrapped with the sludge is a good soil conditioner, it is relatively damaging to pumps and the cloths on the vacuum filters. Analytical results were collected from the Lederle treatment works in 1949-50, but this was before installation of the third trickling filter and the final clarifier. The following averages were found: raw wastes - 2,170 mg/l BOD and 1,330 mg/l TSS; and the filter effluents - 812 mg/l BOD and 225 mg/l TSS (18, 101).

By the late 1950's, the Lederle waste treatment plant had been expanded into a two-stage trickling filtration system. The trio of 31 m (100 ft) diameter filters in parallel had become the primary biological stage, whereas a single 41 m (135 ft) diameter filter, served as the second stage. This modified trickling filter facility was designed to operate with a recirculation ratio of 3:1.

Mauriello in 1958 (67) cited prevailing odor problems associated with the treatment plant. The anaerobic condition of the filters during excessive loading represented one odor source of considerable concern. Corrective measures included better flow equalization, increased recycling of partially treated flows, more aeration capability and possible addition of cooling towers to the system. Greater control over concentrated wastes coming down to the treatment plant was emphasized, especially concerning solvent recovery wastes, and spent fermentation beers (which were no longer being dried for animal feed supplements). Also suggested was separate treatment of intermittent small batch amounts of deleterious waste.

Biologicals

Eli Lilly Greenfield Laboratories, Greenfield, Indiana

In 1960, Howe explained that this type of pharmaceutical facility, which produces antitoxins, antisera, vaccines and other substances for the prevention and treatment of specific diseases, generally yields large quantities of potent wastes (6). At Greenfield, Howe indicated that the veterinary and plant science research and production wastes were pretreated before passing to the main treatment works. Pathogenic wastes were separately pasteurized, and the toxic wastes were pretreated with lime and hypochlorite. The antitoxin and vaccine wastes were taken directly to the main treatment facility consisting of primary settling, biological filtration, final settling, sludge digestion, and chlorination. Animal wastes were handled by 8 m^3 (2,000 gal) septic tanks and absorption fields. Various waste solvents, screenings, animal carcasses and miscellaneous solids were collected and taken to incineration facilities for final disposal.

The combined wastes went to an Imhoff tank; the overflows passed to a trickling filter then a final settling basin. Sludges from the Imhoff tank went to drying beds. Secondary-settled sludges and drainage from the sludge drying beds were pumped back to the head of the treatment system. Sludges off the drying beds were either disposed of on land or incinerated with trash, egg solids, manure and miscellaneous solids. The Company encouraged the use of spoiled eggs by nearby hog farmers to decrease the wasteload on the treatment plant (31).

Animals inoculated with pathogenic micro-organisms were isolated, and after autopsy the bodies were incinerated. Pathogenic wastewaters from the isolation holding areas and the autopsy building were discharged into a collection and holding chamber for future steam sterilization at 93°C (200°F) and 30 minutes minimum detention. Effluents from the collection chamber were pumped to the main treatment plant.

Toxic wastewaters from herbicide, insecticide and other research were collected and given separate batch treatment before release to the main treatment plant. Dichromate solutions were reacted with ferrous sulfate and lime to reduce hexavalent chromium to the trivalent form. Phenolic wastes were reacted with lime and hypochlorite. Waste DDT and other insecticides together with solvent carriers, if available in appreciable quantities, were collected in cans and then burned.

Wastewaters associated with the production of smallpox, typhoid and other vaccines were released to the central treatment works. If waste eggs could not be given away to nearby farmers, the eggs were crushed and screened with the egg fluid passing to the treatment works. The screenings and egg shells were burned or buried with other wastes. Sanitary waste from the 200 employees at Greenfield was also discharged to the central treatment plant.

The main treatment works in the late-1950's reflected some expansion from the early 50's, including provisions for prechlorination, a primary clarifier, and conversion of the previous standard-rate trickling filter to a high-rate filter. The primary settler was 53 m^3 (14,000 gal) and the final settler 27 m^3 (7,000 gal), both quite small. Final chlorination remained optional (31, 70). Waste loads entering and leaving the treatment facility during the late 1950's are shown in Table VIII-5.

Bloodgood (53) in 1966 described the next stage in progression of the Greenfield Laboratories. Employment increased to 500 persons and, besides main production capabilities, four peripheral areas of research were added: veterinary science, animal nutrition, plant science, and human medicine. New construction was initiated to conduct toxicity studies and tissue culture work in the area of human medicine. Bloodgood describes the new Greenfield installation as comprising five separate waste treatment plants, i.e. Plants 238, 237, 236, 226 and 219. Plant 219 is the largest of these facilities and is essentially the same as described above consisting of a primary clarifier, a high-rate trickling filter, secondary clarifier and sludge digester.

Table VIII-5

Eli Lilly Greenfield Laboratories' Wasteloads (70)

Influent	Flows				BOD			TS			Settleable Solids	
Plant Area	Avg (m^3/day)	Avg (gpd)	Max (m^3/day)	Max (gpd)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	(kg/day)	(lb/day)
Antisera/antitoxins production	204	54,000	655	13,000	200-400	45-73	100-160	760-1,520	154-308	340-680	41-77	90-170
Additional anti-influenza vaccine production	250	66,720	383	101,000	40-80	9-23	20-50	100-200	27-50	60-110	4.5-14	10-30
Plant science and animal research	204	54,000	708	187,000	810-1,620	186-367	410-810	1,220-2,450	249-499	550-1,100	64-354	140-780
Monkey storage areas	18	4,700	83	22,000	800-1,600	14-27	30-60	770-1,540	136-272	300-600	136-272	300-600
Total (avg)	680	179,400	1,820	480,000	380	254	560[a]	860	567	1,250[a]	122	270[a]

Effluent Parameter	Present (late-1950's)	Future
BOD mg/l	18-40	10-20
TSS mg/l	20-60	20-40
TS mg/l	400-475	400-450
Coliform plate count	400 to 1,000/100 ml	400 to 1,000/100 ml
pH	7.3 to 8.0	7.3 to 8.0

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[a] Maximums of 1,080 lb/day BOD, 2,690 lb/day TS, and 1,080 lb/day settleable solids

Plant 219 affords both primary and secondary treatment principally serving the older portions of the facilities. Animal wastes constitute a major part of flows received into this treatment works. Flows average 303 m^3 (80,000 gpd) with influent and effluent BOD's of 105 mg/l and 35 mg/l, respectively. Steam-sterilized pathogenic wastewaters from animal isolation sectors, which were cited above as entering the plant sewer, actually enter the Plant 219 system. Treated flows from Plant Systems 219 and 226 (described below) are combined, giving 946 m^3 (250,000 gpd) to 1,140 m^3 (300,000 gpd) of effluents with an average BOD of 13 mg/l. Final composite discharges in the mid-1960's were estimated at about 1,140-1,320 m^3/day (300,000 to 350,000 gpd). Bloodgood (53) stated that they were prepared to handle up to 3,780 m^3 (1 mgd) of total wastewater flow in the future at this location.

The other treatment systems primarily handled animal wastes including excreta, spilled feeds, washings and other losses, arising from horses, cattle, calves, pigs, rabbits, mice, monkeys, dogs, and cats. The wasteloads vary from 0.8 to 78 l/day (0.2 to 20.0 gpd) per animal and from 0.007 to 2.9 kg (0.016 to 6.50 lb) BOD/day/animal, ranging from the smallest to the largest animals. Wastewaters from "normal" animal holdings are discharged into 7,600 l (2,000 gal) septic-holding tanks; excess overflows are discharged to absorption trenches within outlying agricultural fields. The septic tanks are cleaned annually or biannually and the resulting sludge is disposed of on nearby lands. The septic tank effluents originating from the "sick" animal isolation barn are diverted into the wet well of the treatment plant for prechlorination and subsequent bio-oxidation. The various peripheral treatment systems are tabulated in Table VIII-6.

Drug Formulation

Merck, Sharpe, and Dohme, West Point, Pennsylvania

In 1951, the West Point facility consisted of the main warehouse, the pilot plant and fermentation area, the boiler house, the research laboratories, the synthetic chemical process building and the blood plasma processing laboratories. Liontas (34) reports that a high-rate trickling filter installation was completed in late 1950 - early 1951 at the West Point pharmaceuticals works. Wastewaters were made up of organic and inorganic acids, fermentation wastes, salts, acidic solvents, and various aliphatic and aromatic organic chemicals. Sanitary wastes were also received into the biological treatment works. From available data, fermentation wastes are thought to comprise only a small portion of the entire plant wasteload.

The plant had three sewer systems: one for storm and cooling waters, one for sanitary wastes, and one for industrial wastes. Storm and cooling waters are discharged directly to the receiving stream. Some of the industrial wastewaters flow directly to the trickling filtration treatment works, whereas others first receive special handling and pretreatment. Pretreatment of selected industrial wastes was intended to protect the biological system. The wastes are essentially

Table VIII-6

Eli Lilly Animal Waste Treatment Facilities
Greenfield, Indiana (53)

Plant	Type and Source of Waste	Treatment
236	Swine Barns	Flow = 19 m^3 (5,000 gpd) est. Influent and effluent BOD = 510 and 75 mg/l, respectively Screening, holding tank (56.8 m^3; 15,000 gal), aerated tank (90.8 m^3; 24,000 gal), settling tank (26.5 m^3; 7,000 gal), final effluent to seepage
226	Toxicology Building, Tissue Culture complex, Agriculture and Industrial Products buildings, Veterinary Isolation Barn, Engineering and Maintenance shops.	Flow = 660 m^3 (175,000 gpd) Segregation of bedding, screening, dual aeration and settling tanks (980 m^3; 260,000 gal), sludges to underground (340 m^3; 90,000 gal) sludge digestion tank, overflows to (1,360 m^3; 360,000 gal) earthen lagoon, cooking of selected pathogenic wastes.
237	Feed mill and wash-downs from chicken barns	Two underground holding tanks in series, first aerated (49.2 m^3; 13,000 gal); second for settling (34 m^3; 9,000 gal); to a stone filter bed then to ground
238	Sheep and cattle barn	Underground tank subdivided into wet well (6.2 m^3; 1,650 gal) and sludge digestion (69.3 m^3; 18,300 gal); from wet well to lagoon (378 m^3; 100,000 gal), final percolation into ground.

equalized, and the acidity is neutralized with concurrent precipitation of sludge containing heavy metals. The sludge slurry is pumped to sludge lagoons for solids concentration. The strong lagoon supernatants and underdrain filtrates, containing about 10,000 mg/l BOD, are sent back to the treatment works. This represents a major load imposed upon the treatment plant.

The waste treatment works consisted of: a two-stage, high-rate trickling filter preceded by a comminutor, primary wet well and primary settling; followed by secondary settling, intermittent sand filtration and final chlorination. Thre was no intermediate settling between the two filter stages, but a secondary wet well was available for waste application to the second-stage trickling filter. A portion of the first stage filter effluent is returned to the primary wet well as recycle to the first-stage filter, the remainder passing to the secondary wet well. Part of the effluent from the secondary settler is returned to the secondary wet well for recycle to the second-stage filter. Nonrecycled effluent from the second-stage filter passes to an alternating dosing chamber which intermittently doses the sand filter beds. Sludges from the secondary settler are drawn into the primary wet well and theoretically removed from the primary clarification unit. The primary sludges are conveyed to the industrial pretreatment equalization/neutralization tanks. The (precipitated) sludges are then sent to the sludge lagoons. Lagoon solids are periodically removed and disposed of (34).

Design of the biological treatment plant was based on the following loading criteria: flow - 380 m^3/day (113,000 gpd); BOD - 1,450 mg/l ~620 kg (~1,360 lb) BOD/day; TSS - 220 mg/l; filter recycle ratio of 3:1 for the primary stage and 2:1 for the secondary stage. The total cost of the treatment plant was approximately $600,000, including the sewers and engineering services. When the facility began operating in November 1950, it received only sanitary sewage. Sludge lagoon supernatants were introduced to the treatment works in September 1951.

During 1952, an average of 330 m^3/day (98,000 gpd) wastewater containing 330 kg (725 lb) BOD/day was sent to the biological treatment works (85 percent of hydraulic design load, but only 53 percent of organic design load). Overall average BOD reduction was greater than 98 percent through treatment, and TSS removal was 91 percent, giving an average of only 2.5 kg (5.6 lb) TSS/day in the final effluents. Annual O&M cost in 1952 was $40,500. It also cost $1.10/1,000 gal waste treated which equates to $4.70/lb BOD removed. These costs were high because full pharmaceuticals production had not yet been reached at West Point.

Elimination, control and/or pretreatment of industrial wastes were closely engineered into the process operations. For example, highly viscous organic chemicals were collected into drums and burned, and blood wastes were incinerated. Once, the pilot plant wanted to discard a fermenter loaded with Terramycin, but the antibiotic would have likely disrupted the biofilters. Since it was found that high alkalinity inactivates the antibiotic, sodium hydroxide was added to the fermenter before discharge to the sewer. Also, the pilot plant can shift complex or difficult wastes to land irrigation or land disposal.

In colder months, such as January 1952, overall BOD removal dropped about 5 to 7 percent below the average. When the plant was starting up recycling was too high, causing significant icing in the system, so the recycle rates during extremely cold weather were reduced. The filters could withstand shock loads with as much as a 200 percent variation in BOD loads from one day to the next. Although the treatment facilities were operating well under the design levels, occasionally the filters were exposed to loadings in excess of twice the design criteria. Large quantities of antiseptics and antibiotics twice reached the treatment system causing appreciable sloughing of the filters, but in a few days conditions appeared to return to normal.

Nitrogen data collected in July 1953 showed a consistent drop in nitrates across the first-stage filter, but then a significant increase occurring across the second-stage trickling filter and the sand filter. Effluents contained 3.3 to 8.2 mg/l nitrate (N) compared to 1.0 to 2.6 mg/l nitrate in the incoming raw wastewater. The Company described the biological treatment works as giving excellent performance (34).

OTHER TREATMENT METHODS

A number of special treatment methods are practiced at pharmaceutical plants. These methods, discussed below, include: *anaerobic filters, spray irrigation, oxidation ponds, sludge stabilization, and deep well injection.*

Anaerobic Filters

Laboratory-scale anaerobic filters were studied by Dennis and Jennett (1) in treatment of pharmaceutical wastes. These strong wastes were ordinarily sent to the city of Springfield, Mo. municipal treatment works. The anaerobic filters were intended to establish pretreatment capacity for the industry prior to municipal discharge. Anaerobic filters were also selected because of the relatively low excess solids generated by such treatment. The waste was found deficient in nitrogen and phosphorous for purposes of biological treatment, so nutrients were added.

COD was used as the major parameter during the study. The waste stream contained about 16,000 mg/l COD, less than 50 mg/l ammonia and organic nitrogen, less than 1 mg/l total phosphorous, 30 mg/l TSS, and trace amounts of heavy metals. The wastewater contained about 1 percent methanol, which accounted for the very high COD concentration. The feed to the filters consisted of the pharmaceutical wastes diluted downwards to between 1,000 to 8,000 mg/l COD.

The soluble wastes could be anaerobically treated without the need for solids recycling. Four plastic columns were used 15.2 cm (6 in) in diameter by 1 m (3 ft) high, each having a 14.3 l (3.8 gal) capacity. The filter media was quartzite stone, 2.5 to 3.8 cm (1.0 to 1.5 in) in diameter. The filters were started up on a mixture of sewage sludge, glucose and nutrients before introduction of the pharmaceutical waste.

Complete conversion to the pharmaceutical wastes was made after about 25 days. Full acclimation was considered achieved when constant gas production and a high COD removal were recorded, which occurred about the 40th day of testing. The feed was brought into the bottom of the filters and the system(s) was maintained at 35 to 37°C (95 to 99°F).

Detention ranged from 12 to 48 hr and organic loads were varied from 0.22 to 3.52 kg COD/m^3 (13.8 to 220 lb/1,000 ft^3) filter/day. Effluent TSS for all filters was generally below 50 mg/l. COD removals were normally 90 percent or more. However, for loads over 1.76 kg COD/m^3 (110 lb/1,000 ft^3)/day the effluent COD's were greater than 200 mg/l and effluent quality was considered deficient. Loading changes caused initial drops (less than 10 percent reduction) in COD treatment, but the filters were capable of readapting nearly to previous conditions within 7 to 21 days. These results demonstrate the ability of the filters to operate successfully under shock loading conditions.

Biological solids taken from the inside of the filter showed very high settleability. The supernantants containd low TSS, and these solids in turn contained less than 3 percent volatile content. Settling of the filter effluent seemed necessary. Although the influent contained small amounts of toluene, this compound was not removed by the anaerobic filters. Furthermore, the toluene imparted a distinct odor which pervaded the treatment system and effluents.

The study concludes that besides low amounts of solids generated, for organic influent loadings in the range studied and at waste strengths greater than 1,000 mg/l COD, the anaerobic filters were capable of COD reductions from 93.7 to 97.8 percent. The filters could be operated for periods up to six months without needing filter solids unloading. The filters also appeared to recover quite rapidly from shock organic loadings (1).

Spray Irrigation

The Upjohn Company, Kalamazoo, Michigan

During the 1950's, severe waste abatement problems led this Company to investigate different treatment methods, one of which was spray irrigation. Excess spent fermentation beers had to be hauled from the plant to external land disposal sites. The merits of spray irrigation were reported by Colovos and Tinklenberg of Upjohn in 1962 (43).

Initial spraying tests, conducted on land behind the manufacturing plant, produced mixed results. In the early tests using straight fermentation beer liquors, odors developed from the beers, from the wind-carried sprays, and from anaerobic ponding. Pretreatment with chlorine was selected as the best means to reduce these odors. Amounts of chlorine found necessary were about 500 mg/l for the steroid beers and 700 mg/l for the antibiotic beers, compared to a total chlorine demand in the range of 1,000 to 2,000 mg/l. These figures indicate high chlorine consumption.

More extensive spray irrigation tests were carried out on unused farmlands about 22.5 km (14 miles) from the plant. The ground cover consisted of the normal weed and grass growths normally found on farmlands in the midwest, not tilled for many years. The upper 20 to 25 cm (8 to 10 in) of soil was a Fox loam (grayish-brown to brown gritty loam), underlain by 25 to 30 cm (10 to 12 in) of yellowish to light brown loam, with 0.3 to 0.9 m (1 to 3 ft) of reddish-brown gravelly sandy clay beneath. After tall grass and weeds had been mowed, a dense ground cover was obtained. Orchard irrigation equipment (aluminum pipe and rotating sprinklers) was used. Chlorinated beers were stored in a 114 m^3 (30,000 gal) underground tank. A maximum of 22 rotating sprayers were employed, each rated at 83 l/min (22 gpm) and with a nozzle pressure of 4 kg/cm^2 (60 psig). The total assembly was capable of handling about 110 m^3 (29,000 gal)/hr of spent beers.

Results of spray irrigation studies were mostly qualitative rather than quantitative. Chlorinated beers were sprayed onto a particular area until the equivalent of about 3.8 cm (1.5 in.) of liquid were applied. The sprays were then transferred to another sector and returned to the original area about one month later. Observations indicated no anaerobic conditions associated with pooling or puddling, which was not true with the unchlorinated beers. An adequate ground cover was considered important in promoting percolation and minimizing runoff. When parched grass was sprayed, the grass recovered rapidly and turned dark green. Areas sprayed in the fall were judged in very good condition the following spring, with very dense and dark green ground cover. Wintertime spraying did not appear to induce any undesirable effects, and no special problems were encountered. Further testing with barley ground cover at the spray application rate of 0.64 cm (0.25 in) per day, or 66 cm (26 in) applied over 5 months gave mixed results, probably indicating an excessive application rate.

Cost of the system exclusive of pumps, storage tank and land was $1,070. Consumption of chlorine was 0.48 to 0.72 kg/m^3 (4 to 6 lbs/1,000 gal) equivalent to $0.05 to $0.08/m^3$ ($0.20 to $0.30/1,000 gal) of spent beer sprayed. Further studies were to include drilling of test wells to discern the presence or absence of ground water contamination, adaptability of other types of ground cover, maximum rates of application, and long-term effects of high chloride content of the wastes on the soils. It was concluded that spray irrigation of spent fermentation beers, based on the evidence gathered up to that time, was proving very satisfactory (43).

Oxidation Ponds

Studies in India

Laboratory and field-scale studies were conducted in India on treating synthetic drug waste mixtures by pure cultures of algae (39). Reported results were somewhat difficult to interpret and therefore only summary findings are given.

In a series of experiments, synthetic drug wastes were diluted with water and settled sewage in the range of 1:100 to 1:2 (drug waste: water + sewage). The objective was to obtain the least dilution whereby the organic and toxic levels would be maximum but still capable of supporting a healthy algae population over a reasonable period of time. Harvesting of the algae was not mentioned.

The various waste mixtures were inoculated with pure cultures of Chlorella pyrenoidosa and Scenedesmus quadricauda. In some cases, acidic pH levels were adjusted before algae inoculation, whereas in other cases it was not. Dissolved oxygen, pH, BOD and color of the waste mixtures were measured at various intervals. Maximum waste holding and treatment was 10 days.

Synthetic drug wastes diluted 20 times with water and settled sewage gave initial BOD's in the range of 120 to 352 mg/l (at 37°C; 99°F) for the various mixtures. S. quadicauda was generally more efficient in waste reduction than C. pyrenoidosa. Interference in some of the DO tests was caused by a deep pink color in the raw wastes due to the presence of p-aminophenol. Fish (species unidentified) were acclimated to the drug waste mixtures and during acclimation could survive at BOD concentrations at about 60 to 65 mg/l. After full acclimation, they were capable of survival in the 1:20 synthetic drug diluted waste mixtures.

In general it was concluded that treatment of these synthetic drug wastes by algae oxidation ponds would be very difficult. At a 1:20 dilution (1 part synthetic drug wastes: 20 parts water + settled sewage), Chlorella and Scenedesmus were kept viable for 5 to 8 days, and BOD's were reduced from 310 to 340 mg/l to 30 to 40 mg/l, or 85 to 93 percent BOD reduction. However, reductions varied widely within the individual experiments.

In view of the large dilutions and land areas required, this treatment method presented some formidable problems, solutions to which were considered expensive (39).

Sludge Stabilization

Lederle Laboratories, Pearl River, New York

In 1953-54, Lederle Laboratories initiated pilot plant evaluations on composting and reusing excess organic sludges from overall process operations (61). Organic sludges accumulated from the fermentation of antibiotics, extraction of active ingredients from animal organs, housing of animals, and sanitary sewage from 4,000 persons, with most of the sludge coming from the secondary treatment works. In the mid-1950's 5 to 9 metric tons (6 to 10 tons) of wet sludge were being processed daily. Given available land, it was hoped that composting would solve sludge disposal problems.

Early results showed that one of the best blends for good composting and suitable physical handling was a mixture of 65 percent treatment plant sludge, 25 percent animal manure, and 10 percent sawdust. Before being added to the compost, the treatment plant sludge was dewatered, using lime, on vacuum filters. Phosphate rock was added to the compost mixture, giving a moisture content from 50 to 60 percent. Both moisture and temperature were important in composting. The materials were repeatedly shreddded, blended and turned over.

In 1955, the Company converted 4 ha (10 acres) of open landfill to full-scale composting. Windrows, made up of shredded, blended and properly-mixed materials, were about 7.6 m (25 ft) wide, as much as 4.6 m (15 ft) high, and ran up to 91 m (300 ft) long. They were allowed to compost for 5 months or longer. The aged compost was eventually trucked into an enclosed building and reshredded, giving a final moisture content of about 40 percent. The windrow method had a capital investment of only about $10,000 and an annual operations expenditure of about $15,000.

In final form the compost was a granular, free-flowing, dark brown material with a slight humus scent. The finished compost was reportedly used on Lederle grounds, by adjoining communities, and sold through a local outlet for lawn treatment and soil conditioning.

By the mid-1960's, organic sludge at Lederle had increased to about 18 metric tons (20 tons) daily, consisting of 10.9 metric tons (12 tons) of wet biological sludge from the 3,785 m^3/day (1 mgd) industrial waste treatment works and 7.3 metric tons (8 tons) as antibiotic cake residues, animal cage wastes and manure (15). Windrowing worked well for some time, but eventually the local commercial product was phased out. Procedures were changed, whereby the compost was held in windrows for up to 2 years and the materials were turned only every 6 months.

Eventually, whether due to production shifts creating greater amounts of acid sludges or, more probably, due to the natural encroachment of homes around the Lederle property, odors arising from the composting became a public problem for the Company. In 1968, the Company turned the piles in the fall and winter and reverted to smaller-sized windrows with more frequent turning. These changes were only partially effective.

After 15 years, composting was to continue, but only if the odor problems could be solved. Economically alternative means of disposal were being sought. Compared to other methods of solid waste disposal, composting has cited advantages of low capital and operations expense, minimal air pollution problems and the conservation of natural materials. Disadvantages include the greater land requirement, potential odors, and the absence of ready markets for the final product. As a fertilizer, unsupplemented compost is rated quite low in N:P:K content, i.e. 2:1:1. Thus for buyer education, emphasis should be placed on compost as providing trace elements, organic matter, chelating agents, and perhaps growth factors that are not found in commercial fertilizers (15).

Deep Well Injection

Parke-Davis Company, Holland, Michigan

At Parke-Davis, concentrated chemical manufacturing wastes are injected by a deep well system into a limestone strata 427 to 518 m (1,400 to 1,700 ft) below ground surface (see Waste Characteristics Section for nature and strength of this waste). Maximum pumping rate of injected chemical wastes is about 163 m^3/day (43,000 gpd) (13, 59).

Before the Company committed itself to the deep well system in the early 1950's, pilot plant studies served to eliminate other waste handling/treatment alternatives including waste neutralization, activated carbon, evaporation of the liquors, and trickling filtration. Since the chemical wastes contained high dissolved salts and had considerable buffering capacity, neutralization was judged too expensive and would not cope with other objectionable properties of the process wastes. Activated carbon could reduce the color level of the wastes from 11,000 Pt-Co units to 2,000 units, but this was still much too high. Activated carbon was also prohibitively expensive in view of the high O&M costs and remaining problems of toxicity and BOD. Evaporation necessitated difficult residue disposal and high fixed and operating costs. However, in the event of a breakdown in the well disposal works, the Company decided to have a converted evaporator system available as a standby. Trickling filter studies indicated at least a 50 percent reduction in BOD, but removal of color, toxicity and salinity were unsatisfactory. It could not compare favorably with deep well disposal chiefly because of high initial investment, the filter may be incapable of handling wastes from new products, and in the event of plant shutdown the filter growths could experience complete dieoff.

In the early 1960's, the concentrated chemical wastes were pumped from the process reactors to a 303 m^3 (80,000 gal) tank for settling. This effluent was cascaded through a second and third 303 m^3 tank, then passed through sand gravity filters and injected underground by a pair of deep disposal wells. Compatibility tests of the wastes with the limestone and brine in the underground formation were conducted before the wells were put into use. The tests have been rerun each time there is a major process change inside the manufacturing plant.

The formation is 10 to 15 percent voids. The Company believes it has benefitted from the large quantity of acetic acid pumped, which has apparently opened up the strata even more. The quality of the chemical waste sewer system is checked with COD rather than BOD tests. Correlations have seemingly been obtained between the COD and the BOD_5 and BOD_{20} results.

The first well is 436 m (1,432 ft) deep and began in 1951. Initial pumping pressure was 21 kg/cm^2 (300 psi) which has dropped to 18 kg/cm^2 (250 psi), and well pressure at rest is 14 kg/cm^2 (200 psi). Production increases necessitated a second well in 1956, which is 503 m (1,649 ft) deep. Initially, the pumping pressure was 21 kg/cm^2 (300 psi) but then rapidly fell to 11 kg/cm^2 (150 psi), and the well pressure at rest is only 4 kg/cm^2 (50 psi). These pressure heads appear abnormally low. The pumps used for waste injection are triplex, positive displacement, porcelain-lined units.

Advantages of the deep well system are reported to be: low cost of installation, maintenance and operation; and complete elimination of hard-to-dispose-of wastes. Reported disadvantages are: what is occurring cannot be seen; a high element of risk if the area has not previously been surveyed by the drilling of several other wells; and the possibility of contaminating the underground strata. The injection well system is reported practical when the waste volume is not excessive, the underground strata has the proper characteristics, chances of underground contamination are slight, the wastes are compatible with and can be adequately assimilated into the strata, and no other method appears possible or feasible to handle the waste problem (13, 59).

A recent appraisal of the Parke-Davis deep well disposal works indicates this system may need to be upgraded with respect to the EPA Administrator's Decision, Statement No. 5, made in 1973 on deep well waste injection. This system, unless supported by additional data, may not be in accord with the present philosophy of alternately treating and disposing of the subject waste by surface means. Past injection history shows that fracturing of the underground strata has indeed occurred, with possibile vertical fracturing of the overlying shale layers or the confining aquaclude.

Abbott Laboratories, Barceloneta, Puerto Rico

Plans in 1968-69 for the new Abbott antibiotics facility in Barceloneta, Puerto Rico more or less stipulated there would be no external waste discharges from the fermentation sectors (22). Spent fermentation beers, mycelium and solvents would be fully recovered. Miscellaneous process wastes like floor washings, ion exchange rinses, and tank cleanings originating from the antibiotics or other processing areas were to be merged with boiler blowdown, tower blowdown and the plant sanitary sewage, and then discharged into deep injection wells. It was reported the only discharges leaving the plant would be clean waters originating as roof drainage, surface runoff occurring during periods of rainfall, and some miscellaneous clean or cooling waters without organic content. The injection well was to be drilled to a sufficient depth until the salt content in the underground aquifer reached a minimum of 5,000 mg/l. The Company was prepared to go to a well depth of 762 m (2,500 ft) costing $100,000. There is strong indication these waste treatment and disposal plans were changed substantially before the startup of full-scale process facilities.

The Upjohn Company, Kalamazoo, Michigan

In the early 1950's, Upjohn's production was greatly outdistancing the capability of its waste treatment facility to handle the wasteloads

(19, 68). The synthesized organic chemicals manufactured included cortisone, hydrocortisone, folic acid, adrenal cortex and other cortical steroid products. The chemical wastewaters with up to 9,070 kg (20,000 lb) BOD/day and considerable organic solvents were discharged to a 36 ha (90 acre) swamp on Company property, a method long obsolete, and producing serious odors. Besides, additional manufacturing of newer steroids was anticipated. The table below shows a preliminary inventory of wastewater discharges from the synthesized organic chemicals manufacturing.

Parameter	Content
Flow	1,510 to 2,650 m^3/day (400,000 to 700,000 gpd)
BOD	2,000 to 10,000 mg/l[a/] = 2,720 to 13,600 kg (6,000 to 30,000 lb)/day
TDS	500 to 7,000 mg/l
pH	2.0 to 8.0, generally acidic
Color	Highly visual
Odor	That of organic solvents

[a/] Waste streams of up to 500,000 mg/l BOD not uncommon.

The liquid waste streams were laden with spent mineral acids and their respective salts, short- and long-chain alcohols, both chlorinated and unchlorinated hydrocarbons, various organic acids, aldehydes, ketones, and the residual fractions of the steroids and their intermediates. The survey showed high variability in wastewater composition from day to day, and new processes and modifications were causing steady increase in the volume and strength of wastewaters. Two programs were undertaken to cope with the pervading waste disposal problems: a preventive waste abatement program; and a search for new waste treatment methods, this phase culminating in a 570 m^3/day (150,000 gpd) deep well disposal system.

Major procedures established under the preventive waste abatement program included:

1. Separating clean spent waters from contaminated wastewaters and discharging the former to the storm sewer
2. Recovering solvents wherever practical
3. Collecting and hauling selected high organic wastes to land disposal
4. Collecting and incinerating non-reusable combustible solvents and residues
5. Exhausting steam jets to the atmosphere
6. Recycling seal waters on the vacuum pump systems
7. Providing bypass bleeder lines on drinking fountains
8. Employing good housekeeping practices such as shutting off drinking fountains during night hours and weekends, turning off hoses when not in use, and repairing leaking valves.

The preventive program was surprisingly effective. From September 1953 to April 1954, the raw chemical wastewater flow was reduced from a peak of 2,840 m^3/day (750,000 gpd) to 284 m^3/day (75,000 gpd). The corresponding drop in daily BOD loads was from 13,600 kg (30,000 lbs) /day at peak to 1,360 kg (3,000 lbs)/day in March-April 1954. Wastewater volume reduction was in large part attributed to the many steam vacuum jets used in manufacturing. These jets were made to discharge to the atmosphere, dispensing with water contact condensers. Reduction in BOD wasteloads was primarily attributed to the newly installed spent solvents incineration system.

During the preventive program, various treatment was evaluated, including biological degradation, evaporation and concentration, underground disposal into the brine strata about 396 m (1,300 ft) below grade, spray irrigation, chemical treatment, carbon absorption, controlled use of the swamp, and hauling all wastes from the site. From these possibilities, and due to the waste volume reduction experienced during the waste preventive program, deep well injection was selected as most feasible.

To start the well program, one test well was drilled and found to have an injection capacity of at least 378 m^3/day (100,000 gpd). Following this, two full-scale waste disposal wells were drilled into the brine strata at respective depths of 467 and 450 m (1,532 and 1,476 ft). This system was designed to dispose of 568 m^3/day (150,000 gpd) of synthesized organic chemicals process wastes (19, 68, 72).

Final segregation and collection of spent flows resulted in the following waste handling and abatement system:

1. 3,785 m^3/day (1.0 mgd) of uncontaminated cooling waters from various coolers and condensers were released to a storm sewer and then to the swamp -- a 36.5 ha (90 acre) existing pond.
2. Strong process and sanitary wastes with an average flow of 284 m^3/day (75,000 gpd) and a maximum flow of 568 m^3/day (150,000 gpd) and containing about 1,810 kg (4,000 lb) BOD/ day, were forwarded to the deep disposal wells.
3. 150 m^3 (40,000 gal)/month of solid waste, including chemical sludge, was hauled away by tank truck and spread onto nearby lands.
4. 11 m^3/day (3,000 gpd) of nonreusable waste solvents directed to a specially designed solvent-incinerator, the waste heat from which was reused for incineration of animal refuse.

In disposing of the strong process wastes, pretreatment was necessary before deep well injection. Liquid wastes were combined in a vitrified tile sewer resistant to acid, alkali and solvents. Pretreatment consisted of pH adjustment with high calcium lime followed by flocculation, settling in a 227 m^3 (60,000 gal) clarifier, a first surge tank of 219 m^3 (58,000 gal), filtration, a second surge tank of 219 m^3 (58,000 gal), and the pump station. A stainless steel vertical leaf

Niagara pressure filter was used for filtration. Diatamaceous earth was used to precoat the filter leaves. Suspended solids were reduced in the prefilter flows from 100 mg/l to less than 10 mg/l in the filtrate. Filter cake was sluiced and combined with chemical sludge from the clarifier to a dewatering pit, the material from which was eventually hauled away by tank truck for field disposal. The final pumping system used two plunger pumps (with provisions for a third pump if necessary) to inject the filtered wastes into the underground formations under operating pressures of 35 to 63 kg/cm^2 (500 to 900 psig). This disposal plant was placed on line in October 1954 and thought to be operating through 1975 (19, 68).

With the development of the deep well disposal system, the natural 36.5 ha (90 acre) swamp or pond which previously received the strong synthesized organic chemical process waste was converted into a large recharge basin. The storm sewer carrying 3,785 m^3/day (1.0 mgd) of uncontaminated cooling water was directed into this pond. About the same time, the Company also developed a 0.47 ha (1.15 acre) artificial recharge pond. Storm and spent cooling waters from the plant were directed into the 0.47 ha (1.15 acre) basin. In 1955, the artificial pond and the natural pond were recharging 9 and 16 percent, respectively, of the installation's total wellwater drawn from groundwater resources (72).

IX. DEVELOPMENT OF EFFLUENT LIMITATIONS

As discussed in previous Sections, data on waste characteristics, production processes, and waste treatment and control practices for 39 plants in the pharmaceutical industry were compiled from literature searches, industry contacts, and plant visits. The industry was divided into five categories based on differences in production processes, final products, and associated waste characteristics. Waste treatment data was reviewed and evaluated and plants that were achieving exemplary levels of wasteload reductions were identified.

From these plants, model systems were selected for each industry category to define the levels of wasteload reduction that are currently attainable by properly designed and operated waste treatment and control systems. Effluent limitations were then developed for waste parameters of significance for each category, based on performance levels of the model systems. This Section of the report describes the model systems for each category and the effluent limitations developed.

EXEMPLARY PLANTS

A number of bulk pharmaceutical manufacturing plants are currently and consistently attaining exceptionally high levels of organic wasteload reduction, as especially measured by removals of BOD and COD. Most of these plants are in the Fermentation/Organic Synthesized Chemicals category.

Fermentation Plants

There are no known plants that employ *only* fermentation processes for the production of pharmaceuticals.

Organic Synthesized Chemical Plants

High-performance plants identified in this category are the Hoffman-LaRoche facility at Belvidere, N.J. and the E. R. Squibb plant at Humacao, Puerto Rico.

Fermentation/Organic Synthesized Chemical Plants

The majority of pharmaceutical manufacturing plants are in this "combined" manufacturing category. The plants have both extensive fermentation facilities and significant organic chemical synthesis capability. Fermentation operations usually account for about 30 to 60 percent of the plant production.

Outstanding plants for this category are: the Pfizer facility at Terre Haute, Ind.; Abbott Laboratories, Inc. plants at North Chicago, Ill.

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and Barceloneta, Puerto Rico; and Eli Lilly's Clinton Laboratories at Clinton, Ind. In addition, Lederle Laboratories, Pearl River, N. Y., and Wyeth Laboratories, West Chester, Pa. achieve high levels of wasteload reductions in their pretreatment facilities prior to discharge to municipal treatment systems.

Biologicals Production Plants

Only a few plants of this type exist and data on waste treatment practices are somewhat limited. No exemplary plants were identified.

Drug Mixing, Formulation and Preparation Plants

No exemplary plants were identified for this category. Waste treatment performance at McNeil Laboratories, Fort Washington, Pa., and Wyeth Laboratories, Paoli, Pa. approached exemplary levels.

AVAILABLE TREATMENT AND DISPOSAL PROCESSES

Of the wide variety of techniques and approaches to waste control, treatment and disposal available in the industry, some of the better adapted and designed systems have performed extremely well. Other systems for a number of reasons are yielding relatively poor results. The industry has employed all of the following aggregated subsystems at one time or another:

- Separate filtration of mycelium, and drying and recovery of fermentation broths and mycelium for use in animal feed supplements.
- Solvent recovery at centralized facilities or at individual sectors. Reuse and/or incineration of collected solvents.
- Collection of biological, synthetic and pathogenic wastes when present, within plant for incineration or disposal by separate means. Included are steam cooking and sterilization of pathogenic wastes, separate dry cleaning of animal cages, and overall animal wastes.
- Special recovery and subsequent sale of sodium sulfate salts.
- Scavenging and recovery of high-level ammonia waste streams, sold in bulk as a fertilizer base and for other needs.
- Elimination of barometric condensers.
- Extensive holding and equalization of wastewaters prior to treatment systems.

- Incineration of mycelium and excess biological sludges. Incineration system may also receive pathogenic wastes, unrecoverable solvents, fermentation broths or syrups, semisolid and solid wastes, etc. System can furthermore be integrated with the burning of odorous air streams. Concurrently, waste systems may be covered or enclosed for odor control and for maintaining optimum temperatures for biological treatment.

- The activated sludge process including multiple-stage, extended aeration, the Unox aeration system, and other variations.

- The trickling filtration process, including high-rate and bio-oxidation roughing towers, and multiple-stage systems.

- Acid cracking at low pH's.

- Extensive neutralization and pH adjustment.

- Spray irrigation of fermentation beers and other pharmaceutical wastes. Other forms of land disposal are employed. Deep burial is unacceptable without the highest possible precautions.

- Treatment of selected waste streams by activated carbon, ion exchange, electro-membranes, sand filtration, chemical coagulation, etc.

- For proper handling and disposal of excess biological sludges, a number of possibilities are available, including sludge flotation, thickening and vacuum filtration, sludge centrifugation, degasification, aerobic and/or anaerobic digestion, lagooning, drying, evaporation, converting into a useable product, incineration, land spreading, crop irrigation, composting or landfilling.

- Anaerobic or submerged filters.

- Cooling towers are necessary at pharmaceutical plants for reuse of cooling and jacketting waters.

- Chlorination, pasteurization and/or other equivalent means of disinfection. Extensive disinfection is generally utilized inside vaccine-antitoxin production facilities.

- Municipal waste treatment.

- Multiple-effect evaporation-steam and/or oil, multiple hearth and rotary kiln incineration, and special thermal oxidation systems.

- Extensive air cleaning by electrostatic precipitators, venturi and water scrubbers and other equivalent systems.

MODEL SYSTEMS

The more advanced waste treatment and control systems at pharmaceutical plants almost invariably include activated sludge or trickling filtration processes, usually as multistage systems, although other suitable treatment processes are available. From all indications, these systems are equally applicable to all types of pharmaceutical plants. With the exception of Eli Lilly's Clinton Laboratories, Ind., Abbott Laboratories at Barceloneta, Puerto Rico, and Commercial Solvents Corporation, Terre Haute, Ind., the known plants all employ some variation of the activated sludge process.

Burgess (47), in 1967 British literature, cites at least two cases where the activated sludge process gives very high organic reductions on pharmaceutical type effluents. Wastes containing phenolics, aldehydes, organic acids or similar compounds generally can be treated economically by biological means with up to 99 percent BOD reductions. A chemical plant, with 70 percent citric acid wastes and 30 percent other pharmaceutical product effluents, employed the activated sludge process in reducing the raw waste BOD from 1,800 mg/l to 50 mg/l BOD; that is equivalent to a 97.2 percent BOD removal. It was also indicated for a chemical plant manufacturing a wide array of pharmaceutical products, dyestuffs and intermediates that two-stage activated sludge could reduce the raw waste BOD from 1,000 mg/l to about 50 mg/l in the final effluents, obtaining a BOD reduction of about 95 percent.

The Upjohn Company, Kalamazoo, Mich., demonstrated successful treatment of spent fermentation beers (category 1) through the 1950's by two-stage trickling filtration. Pharmaceutical raw wastes amounting to 2,270 m^3 (600,000 gal)/day and containing 1,397 kg BOD (3,080 lb)/day were reduced by trickling filters to about 41 kg BOD (90 lb)/day in the final effluent, equivalent to BOD reductions of 95 to 98 percent. Influent and effluent BOD concentrations were respectively 600 mg/l and 20 mg/l.

Wastes from Merck and Co., West Point, Pa. (categories 5 and 1) in the 1950's were subjected to high-rate trickling filters giving high treatment performance. Overall BOD reductions were reported as greater than 98 percent and TSS removals about 91 percent.

Throughout 1972, the Stonewall, Va. plant of Merck and Co. (category 3), utilizing three-stage biological treatment and with relatively high raw wasteloads, showed average annual BOD and COD removals of 95 and 80 percent, respectively.

Spray irrigation is relied on as the principal means of waste treatment and disposal at the Commercial Solvents Corporation (CSC) plant, Terre Haute, Ind. (category 3). Including a series of waste connections to the city, CSC accomplishes 91 percent BOD reduction. This is noteworthy because 9 percent of the raw wastes receive no treatment whatsoever.

Another interesting case is the E. R. Squibb plant in Puerto Rico (category 2). According to Company reports, more than 99 percent of the total organic raw wasteloads from this plant were to be incinerated, amounting to 30,840 kg COD (68,000 lb)/day. A dilute process stream would be subject to biological treatment, producing a final effluent of no more than 23 kg COD (50 lb)/day.

The model systems presented below detail the unit processes used at each high-performance plant and the associated wasteload reductions.

Organic Synthesized Chemical Plants

Treatment steps at the Hoffman-LaRoche facility at Belvidere, N. J. include the following:

- Screening
- Pre-clarifier
- Equalization basin equipped with turbine aerators, providing about a 1-day waste detention time
- pH adjustment and/or neutralization
- Flocculator-clarifier
- Activated sludge aeration
- Secondary settler
- Two shallow oxidation ponds in series
- Sludge thickening tank
- Aerobic sludge digestion tank and sludge drying beds
- Final chlorination
- Sodium sulfate recovery system, a very unique feature that includes a fluidized bed process and an anhydrous sodium sulfate plant

Limited treatment results have been received for the Hoffman-LaRoche system. Based on treatment plant design and Company data of Sept. 1973, minimum BOD reductions are calculated to be in range of 96.4 to 98.1 percent (average of 97.5 percent for BOD), and TSS removals in the range of 90 percent. Design criteria called for BOD and TSS reductions of 97.4 and 98.0 percent, respectively. COD removals of at least 90 percent are apparently being attained. Other data show that effluent phosphorous and ammonia loads are exceptionally low.

Fermentation/Organic Synthesized Chemical Plants

The waste treatment system at the Pfizer, Inc. plant in Terre Haute, Ind., is essentially a five-stage biological system with a retention time for process wastes of 45 to 65 days. Both the activated sludge and trickling filter processes are used. An extensive case history on this plant is presented in the Appendix. System components are as follows:

- Primary settling
- Two extended aeration (activated sludge) basins, generally operated in series, providing up to 12 days' waste retention
- Secondary settling

- Two clarigesters in parallel
- Two standard-rate trickling filters in parallel
- High-rate bio-oxidation tower
- Final clarifier
- Two 2 ha (3.75 acre) aerated stabilization ponds in series
- 17 ha (35 acre) stabilization pond
- Chlorination
- Aerobic sludge digester
- 20 ha (40 acre) sludge stabilization pond
- Land and crop application of stabilization pond sludges
- Holding pond giving 1-day detention of spent cooling waters

In 1972, Pfizer reported average BOD and TSS waste removals through the treatment works of 98.0 and 97.5 per cent, respectively. Analysis of data for 17 consecutive months through May 1974 showed average waste reductions over this period of 99.1 percent for BOD and 97.8 percent for TSS. The treated process stream averaged 10 to 15 mg/l BOD and 20 to 30 mg/l TSS. Including the untreated cooling water flows, minimum waste removals were about 98 percent for BOD and 95 percent for TSS. The Pfizer system was capable of giving 50 percent phosphorous removals. Unoxidized nitrogen levels in the raw process wastes were high, but the biological treatment works provided average removals in Kjeldahl, ammonia, and organic nitrogen wasteloads of 75, 67 and 81 percent, respectively. Summer nitrogen removals were significantly higher than winter removals.

Waste treatment system components at Abbott Laboratories, North Chicago, Ill., include the following:

- Waste screening and neutralization
- Two equalization basins providing 1.0 to 1.5 days' waste detention, equipped with auxiliary aeration
- Six 380 kl (100,000 gal) activated sludge aeration compartments equipped with sparged air turbines
- Degasification chambers for the mixed liquors
- Two final settlers in parallel
- Pasteurization of final process effluents
- Chlorination of combined process plus spent cooling water flows
- Evaporation and drying of spent fermentation broths
- Complete enclosure of waste treatment works except for secondary settlers
- Centrifuging of excess biological sludges
- Ducting of odorous air streams from waste treatment works and from fermentation sectors into the main plant boilers
- Incineration of excess biological sludges together with odorous air streams in the main plant boilers
- Recovery of selected waste stream(s) high in ammonia for bulk fertilizer sales
- Spill control program, including diversionary dikes and curbing around tank farms and other critical plant areas
- Provisions to connect highly treated process wastes to the Gurnee, Ill. municipal advanced waste treatment plant in the near future

Data for 1972 at Abbott Laboratories showed average BOD and TOC removals from the process waste streams of 94.6 and 86.0 percent, respectively. In 1973, average BOD and TOC reductions were 96.7 and 83.0 percent, respectively. If one considers the spent fermentation beers going to the evaporators (with a BOD load of 9,000 kg or 20,000 lb/day) as being an equivalent part of process raw wasteloads, average BOD reductions for 1972 and 1973 would then equate to 97.8 and 98.7 percent, respectively. Removals of TSS were in the 71 to 74 percent range, but if the spent fermentation beers had been accounted for as part of the TSS raw wasteloads, equivalent TSS reductions would have exceeded 80 percent. Total phosphorous and ammonia nitrogen loads in the final Abbott effluents were low during 1972-73, averaging 36 kg (80 lb)/day and 156 kg (345 lb)/day, respectively.

The waste treatment and control system at Eli Lilly's Clinton Laboratories, Ind., is unique in that it almost entirely relies upon chemical destruction processes rather than biological processes. The system consists of the following:

- Concentration of waste streams within the manufacturing sectors down to minimal volumes
- Over-sized strippers for solvent recovery
- Stripper system to precondition the wastes entering multiple-effect evaporation
- Carver-Greenfield multistage, oil-dehydration, steam evaporator system receiving strong fermentation wastes
- Two John Zink thermal oxidation incinerator systems receiving highly concentrated chemical wastes
- Bartlett-Snow rotary kiln incinerator receiving plant trash and fermentation mycelium
- Small biological treatment plant for handling sanitary sewage
- Extensive cooling water towers and cooling water recirculation systems
- Scrubbing of air effluents from all incinerators and from the waste heat boiler on the Carver-Greenfield system

Clinton Laboratories is currently achieving 90 percent or better removal of both BOD and COD from its raw wasteloads. Minor treatment modifications in the future, however, are expected to increase overall reductions up to 95 percent for BOD and 93 percent for COD. The Clinton plant continues to demonstrate COD reductions equivalent to BOD reductions. The COD to BOD ratio for the final effluents is surprisingly about 2.2, almost the same as for the incoming raw wastes. An extensive case history of this plant is presented in the Appendix.

Other treatment and control systems in the pharmaceutical industry have also produced high treatment performance results for this category of wastes. Two of these systems provide extensive pretreatment of wastes prior to discharge to municipal treatment systems. Wyeth Laboratories at West Chester, Pa. consistently showed 90 percent BOD removal, and up to 90 percent COD removal in the 1960's with an activated sludge plant. Lederle Laboratories at Pearl River, N. Y. with the Unox aeration system and the activated sludge process is currently demonstrating slightly over 90 percent BOD reduction. The additional secondary treatment of these highly treated effluents provided by the municipal systems is thought to give overall BOD removals of 97 to 98 percent for Wyeth pharmaceutical wastes, and about 97 percent BOD reductions on Lederle's wastes.

Biologicals Production Plants

No exemplary plants were identified for this category; therefore, no model system could be specifically defined. A case history giving details of the treatment system for the Wyeth Laboratories at Marietta, Pa., a serums, vaccine and antitoxins production plant, is presented in the Appendix. Unfortunately, the activated sludge treatment plant at Wyeth, Marietta was experiencing possible overload and toxicity difficulties. Reductions in BOD averaged 92.3 percent, but BOD results were likely affected by toxicity; COD reductions were only about 50 percent. This was not an exemplary treatment situation. The data base for this category is relatively limited because very few of these plants exist. Good waste treatment performance is cited elsewhere in the report for Eli Lilly Greenfield Laboratories, Ind. (category 4). Waste treatment removal efficiencies have also been high at Lederle Laboratories, which in part is also a category 4 plant. Technical judgement based on the literature and field experience indicates that waste treatment results comparable to those achieved by category 5 plants (described below) should be achievable by this category.

Drug Mixing, Formulation and Preparation Plants

Two plants were identified in this category that have waste treatment systems that approach but do not attain exemplary levels of wasteload reduction. Both showed reasonably good waste removals with rather small, compact activated sludge plants.

The treatment system at the Wyeth Laboratories, Paoli, Pa. includes the following components:

- Screening
- Two equalization basins equipped with auxiliary air spargers, providing up to 2 days' waste detention
- Three activated sludge chambers operating in parallel
- Secondary settling
- Aerobic digestion of excess biological sludge with residues taken to sanitary landfill
- Chlorination of final effluent

During the period Jan. 1973 to Jan. 1974, the treatment system BOD and COD removals averaged 94.5 and 85.0 percent, respectively. A case history of this plant is in the Appendix.

At McNeil Laboratories, Fort Washington, Pa., process and sanitary waste streams are segregated and receive separate handling before passing through an activated sludge system. Treatment system components include the following:

Process Wastes

- Primary settling tank
- Two equalization basins equipped with auxiliary air and providing waste retention up to 2.5 days

Sanitary Sewage

- Comminutor

Combined Wastes

- Activated sludge chambers, 24 hr aeration
- Two secondary clarifiers in parallel
- Chlorination of final effluent
- Provision for sludge recycling around the aeration chambers
- Thickening and aerobic digestion of excess sludges

In spite of hydraulic and organic overload conditions, the McNeil system over the period Jan. 1973 through Jan. 1974 achieved average waste removals of 92.4 percent BOD and 87.7 percent COD. Without overloading, the system could likely have produced about 95 percent BOD removal and 90 percent COD removal.

EFFLUENT LIMITATIONS

The end products of the compilation, review, and evaluation of the data presented in this report are effluent limitations. They are used as the basis for specifying numerical limits on the allowable wasteloads that may be discharged from individual pharmaceutical plants. In most industries, effluent limitations have been developed that specify an allowable wasteload per unit of production. It has been inferred throughout this report that waste limits per unit of production could not be established due to: the wide diversity and large number of products made; the trading of intermediates between plants; lack of agreement in the industry concerning what to measure and how to measure products; and extreme reluctance of the pharmaceutical companies to disclose appropriate production data. The effluent limitations developed herein are thus specified in terms of percentage reductions in raw wasteloads or final effluent concentrations appropriate for each parameter of significance.

Limits for BOD, COD and TSS

Wasteload reductions achieved by high performance plants varied only slightly between systems handling wastes from organic synthesized chemical plants (category 2) and systems treating wastes from plants with a large component of fermentation processes (category 3). Demonstrated BOD removals ranged from 96 percent for fermentation operations to 94 percent for organic synthesized chemicals. Comparable variation in COD reductions were 83 vs 81 percent. No difference in TSS removals was observed. Effluent limitations for fermentation (category 1), organic synthesized chemicals (category 2), and fermentation/organic synthesized chemical (category 3) plants were set at 95 percent BOD removal, 82 percent COD removal and 82.5 percent TSS removal. For category 3 plants, a refinement in effluent limitations can be made by determining the percentage production of pharmaceuticals by fermentation vs organic synthesis and adjusting BOD and COD limits between the two sets of values noted above.

For biologicals production plants (category 4) and drug mixing, formulation and preparation plants (category 5), effluent BOD and COD limitations were established as 92.5 and 80 percent removals, respectively. Proper data were not available on which to base broad TSS limits.

The detailed information given in this report indicates that in applying suitable treatment processes the BOD, COD and TSS limitations can be reached with a wide degree of flexibility, certainty, and a considerable margin for safety. Maximum daily limitations are recommended as 2 times the average daily limits for BOD and COD, and 2.5 times for TSS. These limits are intended in all cases to represent baseline or minimum requirements.

Ammonia Nitrogen Limits

Pharmaceutical plants that have fermentation or organic synthesis operations generate large loads of unoxidized nitrogen (ammonia and organic nitrogen). Ammonia nitrogen limits are generally necessary for plants in categories 1, 2 and 3 because effluents from these plants even after biological treatment may still contain thousands of pounds per day of unoxidized nitrogen. Ammonia and organic nitrogen loads for certain plants have been shown to exceed BOD loads in the final effluents.

Oxidation of ammonia to nitrate nitrogen can theoretically consume about 4.6 parts of oxygen for each part of ammonia present in wastewaters in comparison to about a 1.4:1 ratio for BOD. Organic nitrogen correspondingly has a high dissolved oxygen demand for oxidation into nitrates. Ammonia is decidedly toxic to fish and aquatic life under varying stream conditions. Also, even moderate levels of unoxidized nitrogen can give distorted results in running the BOD analysis on plant effluents. And finally, chlorination of effluents containing ammonia and other organic nitrogenous compounds can form chloramines and associated compounds that can, in turn, be highly toxic to fishlife, impart off-tastes to water supplies, and create other undesirable side effects.

Based on intensive discussion with industry members over the past few months and practical considerations, effluent limits for ammonia nitrogen were established as 25 percent of existing plant discharges (i.e. 75 percent reduction), or 100 mg/l times the internal plant process flows, whichever gives the lesser amount. The level of 100 mg/l can be reached by in-plant controls, scavenging and process substitution in most factories. There would therefore be no need for extensive treatment. Ammonia levels of 20 mg/l times prevailing process flows are technically achievable and at least one industry member has indicated tentative concurrence with the 20 mg/l limit. The lower limit may ultimately be specified for the industry in the future.

Limits on Metals and Trace Ions

Because of their presence in most pharmaceutical effluents, metals and trace ions have been indicated as being troublesome. Limits for metals have indeed been set on a number of actual NPDES pharmaceutical permits. Individual plant conditions will often dictate particular allowable limits; consequently only suggested effluent limits are given here. Previous pharmaceutical permits have employed the following ranges: iron - 1.0 to 1.5 mg/l; manganese - 0.5 to 1.0 mg/l; phenolics - 0.25 to 0.5 mg/l; total chromium - 0.25 to 0.5 mg/l; aluminum - 1.0 to 2.0 mg/l; sulfides - about 0.5 mg/l; zinc - 1.0 to 1.5 mg/l; lead - 0.1 to 0.25 mg/l; copper - 0.5 to 1.0 mg/l; and mercury (total plant) - 0.05 kg (0.1 lb)/day.

Other effluent limits may be equally appropriate depending on specific conditions and the type of facility involved. Additional constituents deserving attention may include: cyanide, copper, tin, cadmium, nickel, arsenic, chlorinated hydrocarbons, pesticides, and Ra-226, gross alpha and beta (the latter only if radionuclides are being handled by the plant).

Other Limitations

Because of the potential toxicity of pharmaceutical plant effluents, a monitoring requirement for toxicity in effluents has been developed. Every six months, the permittee shall supply TL_m-96 hr bioassay test results for the effluent from each outfall. Fecal coliforms in pharmaceutical effluents shall not exceed 200/100 ml and 400/100 ml, respectively, on an average and maximum daily basis. Maximum temperatures shall also be evaluated at least during the summer months for possible receiving stream impacts. A general stipulation exists that the pH of the final discharges shall always be maintained in the range of 6.0 to 9.0.

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PHARMACEUTICAL INDUSTRY

CASE HISTORY A
ELI LILLY AND CO., CLINTON LABORATORIES
CLINTON, INDIANA

(FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PRODUCTION)

ELI LILLY AND CO., INC., CLINTON LABORATORIES, CLINTON, INDIANA
(FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PLANT)

BACKGROUND

Eli Lilly operates a large bulk pharmaceutical plant at Clinton. The highly automated plant is one of the newest in the industry, having been completed about 1971. The facility was described in 1970 (108,110) as a $60 million complex with $6 to 8 million attributed to "environmental control measures." The plant operates continuously with current employment slightly more than 500. Employment is expected to reach 1,000 by the end of 1976.

Permit applications submitted by the Company in 1971 and 1974 indicated that the plant is engaged in the manufacture of bulk uncompounded antibiotics and medicinal organic chemicals and their derivatives. The plant primarily manufactures cephalosporin antibiotics, a new type of human broad-spectrum antibiotics directed to the treatment of respiratory, urinary tract, and skin and soft tissue infections and diseases which in many cases are reported not to be effectively treated by other antibotics. The cephalosporins are believed to be a highly modified and restructured form of penicillin. Major products made at Clinton are as follows:

-- Monensin Sodium, the desired ingredient in the registered trademark product, "Coban." Coban is prepared in bagged form as a medicated premix for use in broiler (chicken) feed. Coban is reported to materially aid in the prevention of coccidiosis.

-- Cephalexin Monohydrate or "Keflex," a semi-synthetic cephalosporin antibiotic intended for oral administration.

-- Cefazolin Sodium or "Kefzol," the cephalosporin antibiotic prepared in the parenteral or injectable form.

Manufacture of these products would indicate that the Clinton Laboratories are heavily involved in both fermentation and the synthesis of organic chemicals.

There are close corporate and manufacturing ties between the Clinton Laboratories and the Eli Lilly Tippecanoe Laboratories in Lafayette, Ind., and headquarters and manufacturing operations in Indianapolis, Ind. Cephalosporin antibiotics and their derivatives are also manufactured in Lafayette, and trading of intermediate products between Clinton and Lafayette is common. For example, a product manufactured in intermediate stages at Clinton may be shipped to Lafayette for further processing, returned to Clinton, and perhaps then sent to Indianapolis for final packaging. In waste materials handling, this same condition exists. Highly concentrated waste materials may be traded between Lafayette and Clinton for final disposal by incineration at whichever facility has maximum capacity. Most final drug packaging and preparation is believed centered in Indianapolis.

Eli Lilly plans to double production at Clinton Laboratories and has asked for increased allocations on waste load discharges to the Wabash River. Full production for current Phase I is expected about the third quarter of 1975. Production levels in mid-1974 were about 60 to 70 percent of full Phase I capacity. With a doubling of full Phase I capacity, Phase II represents significant expansion both in terms of processing and treatment. Phase II operations are expected to come on line by the 4th Quarter 1975 or 1st Quarter 1976 and will extend through the first part of 1977. The NPDES permit has been written for Clinton Laboratories in staged sequence to cover both Phase I and II production schedules through June 1977.

WASTE TREATMENT AND CONTROL

Plant water supply obtained entirely from Company wells is used for sanitary needs, boiler feed makeup, process cooling water, makeup for cooling water recycling systems in the purification and fermentation process sectors, process needs, and sprinklers.

Treatment Plant design data were based on the following estimated characteristics of waste streams from the manufacturing areas.

Table A-1.
Design Waste Loads (108,110)

Wastes	Load		BOD	
	(kkg/day)	(1,000 lb/day)	(kkg/day)	(1,000 lb/day)
Mycelia	>32	>70	>115	>253
General Plant Trash	5	10		
Concentrated Chemical Wastes				
Primary Wastes	17	38	42	93
Secondary Wastes	48	106	10	23
Dilute Chemical Wastes	54	120	2	4
Watery Process Waste	309	681	11	25
Sanitary Sewage	337	743	0.1	0.2
Untreated Clear Water Stream	23,150	51,041	0.1	0.2
TOTALS	∿23,950	∿52,800	∿180	∿398

The maximum BOD discharged to the Wabash River was estimated in 1970 as 1,100 kg (2,500 lb)/day. The potential raw waste load was claimed by Eli Lilly as amounting to 181,000 kg (400,000 lb) of BOD daily equivalent to the BOD in raw sewage discharged by a city of 2.5 million persons. The Clinton waste reduction system was declared to have a maximum BOD reduction of 99.4 percent.

Design waste handling objectives included: 1) recovery of solvents and process chemicals even if recovery proved uneconomical: 2) no burial of organic wastes either on or off the 280 hectare (700 acre) Clinton industrial site; and 3) no deep well waste disposal. These objectives resulted in the development of a waste handling, treatment and disposal scheme at Clinton that is rather unique in the industry (108,110). In contrast to most pharmaceutical plants that primarily use biological oxidation procedures for treatment of "conventionally" dilute wastes, Clinton uses chemical destruction techniques. Concentrated semi-solid, semi-liquid and liquid waste streams are mostly converted into innocuous gaseous emissions by stripping, distillation, evaporation and incineration. In most plants, the concentrated semi-solid and semi-liquid wastes are transferred off-site for ultimate disposal or separated from the treatment plant.

Mycelia and Plant Trash

Mycelia recovered from the fermentation broths is burned with plant trash. About 136 kkg (150 tons) of wet mycelia equal to 32 kkg (35 tons) of dry product are recovered daily. The extremely high load of 115 kkg (253,000 lb) of BOD/day associated with this waste [Table A-1] is undoubtedly due to the presence of other organics in addition to mycelia. Future plans call for evaporating and converting the mycelia into a dried, high protein animal feed supplement (108,110).

Incineration of mycelia and trash is accomplished in a Bartlett-Snow rotary kiln incinerator equipped with an afterburner and wet scrubber. Ashes amounting to 270 kg (600 lb)/day are buried on site (108,110). Air scrubber effluent is discharged to plant sewers. At full Phase I operational levels, this effluent would have a flow rate of 760 l/min (200 gpm) and would contain estimated daily COD and BOD loads of 54 kg (120 lb) and 18 kg(40 lb), respectively. These incinerated wastes are not normally considered part of the raw waste loads received by treatment works at pharmaceutical installations.

Chemical Wastes

Two types of concentrated chemical wastes are identified in Table A-1. "Primary" wastes are defined as those wastes capable of supporting combustion while "Secondary" wastes require supplementary fuel for burning. These wastes originate primarily in the chemicals manufacturing and purification operations. Some are semi-solid, and even solid. These concentrated wastes have a flow rate of about 61 l/min (16 gpm)(108,110).

Dilute chemical wastes with a flow rate of about 38 l/min (10 gpm) originate as bottoms off solvent stripping columns and other unrecoverable wastes. Lilly has reported that some solvent streams containing about 3 to 5 percent solvents are uneconomical to recover and are mixed with the chemical waste streams.

Both the concentrated and dilute chemical wastes are sent to two John Zink thermal oxidizers equipped with adjustable venturi scrubbers for removal of particulates prior to stack discharge (108,110). Scrubber effluents totaling about 760 l/min (200 gpm) and containing a COD load of about 140 kg (300 lb)/day equivalent to about 90 kg (200 lb)/day of BOD at full Phase I levels are discharged to plant sewers.

The two John Zinc incinerators receive relatively small amounts of wastes but these are extremely concentrated. At full Phase I operations, the quantity of wastes entering the thermal oxidation system is only 76-95 l/min (20-25 gpm), but BOD and COD strengths of these materials assay a few hundred thousand mg/l. It is fairly evident that practically all of the material sent to the John Zink units cannot be considered as normal raw waste loads even under highly unusual conditions in the pharmaceutical industry. In addition to Clinton wastes, highly concentrated wastes from other Eli Lilly plants are incinerated in the John Zink units.

Watery Process Wastes

Watery process wastes, defined as those containing no components more volatile than water, originate primarily from the fermentation operations. The Company would not verify the possible presence of fermentation broths in these waste streams. These wastes, with a flow rate of about 247 l/min (65 gpm), are decanted and then discharged to a Carver-Greenfield evaporation system discussed below.

A stripper operation, associated with the evaporator system, serves the fermentation and product sectors primarily for the reclaiming of solvents from fermentation broths. The stripper system discharges recovered solvents, watery wastes that go to the Carver-Greenfield unit, and a distillate that goes to the plant sewer. The volume of the distillate has not been given but it is expected to contain COD and BOD loads of 320 and 140 kg (700 and 300 lb)/day, respectively, under full Phase I conditions. Because of the extremely large volumes of solvents entering the stripper system, BOD and COD loads in the influent are enormous. This process stream (except for residuals) cannot normally be considered as a raw waste at pharmaceutical plants.

The Carver-Greenfield unit uses a multi-step oil dehydration process and is equipped with a centrifuge, waste heat boiler and a venturi scrubber. Under full Phase I operation, the raw waste load to the unit is predicted to be about 14,900 to 17,400 kg (32,800 to 38,300 lb) COD/day or 7,700 kg (17,000 lb) BOD/day. This unit relies upon an oil carrier stream that is continuously blended into the evaporator and waste heat boiler. The oil carrier stream contains loads of about 5,170 to 6,030 kg (11,400 to 13,300 lb) COD/day equal to about 2,270 to 2,720 kg (5,000 to 6,000 lb) BOD/day. Dehydrated solids from the evaporator are burned in the waste heat boiler to produce steam. Three waste streams leave the Carver-Greenfield unit. The primary effluent is a distillate with exceptionally high organic waste concentrations. Under full Phase I conditions this 150 to 230 l/min (40 to 60 gpm) waste flow is expected to contain 1,500 to 1,720 kg (3,300 to 3,800 lb) COD/day or about 770 kg (1,700 lb) BOD/day. From January to July 1974, COD levels in this effluent were in the range of 1,500 to 2,450 mg/l. This waste stream contains the largest waste load from the Clinton facilities continuing to be discharged to the Wabash River. The waste heat boiler produces about 270 to 320 kg (600 to 700 lb) of ashes daily. Bottom ash is hauled to landfill while flyash is collected in a venturi scrubber and washed to the sewer. This scrubber effluent will contain about 64 kg (140 lb) COD/day or 18 kg (40 lb) BOD/day in a flow of 190 l/min (50 gpm) at Phase I operational levels.

Solvents

Barometric condensers are virtually absent at the Clinton Laboratories. Published information states that approximately 80 percent of the solvents from chemical manufacturing and purification were being recovered by evaporation, distillation and other processes and the Company was attempting to increase this recovery up to 90 percent. Some of the major solvents included benzene, acetone and ethanol. Unfortunately, in the critical area of solvent recovery, much higher efficiencies should be attained by Clinton (108, 109, 110).

Sanitary Wastes

Sanitary wastes are received into a small 379 m^3/day (100,000 gpd) "package" sewage treatment plant that represents the only biological treatment unit present in the Clinton operations. The sewage flow approximates 57 to 114 l/min (15 to 30 gpm) and design BOD input and output loads were rated at 68 kg (150 lb)/day and 7 kg (15 lb)/day, respectively, for this unit at full Phase 1 plant capacity. Aerobically-digested excess sludges from this sub-system are sent to the John Zink thermal oxidizers.

Cooling and Storm Water

Various cooling water streams and storm water from all quadrants of the plant ultimately are discharged without treatment through the main plant outfall (Outfall 001). The Company reports that the daily BOD load contributed by these wastes ranges from 34 kg (75 lb) during dry weather to 68 kg (150 lb) during wet weather with an average of 45 kg (100 lb).

In summary, residual waste discharges from the Clinton Laboratories' chemical wastes destruction facilities consist of the scrubbing effluents from the two John Zink incinerators, the Bartlett-Snow incinerator and the Carver-Greenfield waste heat boiler; the concentrated distillates leaving the Carver-Greenfield evaporator; effluent from the stripper operation preceeding the Carver-Greenfield evaporator; effluent from the sanitary sewage treatment plant; water treatment plant effluents; blowdowns from the extensive cooling water circuits (i.e. having 20,000 to 40,000 gpm recycle) and other blowdowns; some floor drain and storm sewer discharges; an array of spent cooling waters; and waters from undefined or undesignated sources. Total effluent flows were anticipated in the range of 12,500 to 22,000 m^3/day (3.3 to 5.8 mgd) containing around 1,130 kg (2,500 lb)/day of BOD.

The sum of the above waste loads predicted under "full" Phase I production capacity approximates 1,090 kg (2,400 lb) BOD/day and 2,180 kg (4,800 lb) COD/day assuming treatment capabilities remain more or less the same as currently existing. It is noted these waste loads are very close to the conditions approved by the State on September 21, 1971 for the Clinton treatment works as discussed in a later section.

Another interesting point with regard to the above loads is that air pollution control scrub streams contribute about 120 kg (270 lb) BOD/day or about 10 to 12 percent of the total effluent loads from the Clinton plant.

A cost summary for the Clinton, Indiana waste treatment facilities prepared by Eli Lilly in 1970 showed, at that time, projected installation expenditures would be around $4.9 million and total costs including depreciation would approximate $1.58 million (108,109,110).

WASTE LOADS

NPDES Permit Application

The initial permit application submitted in July 1971 gave the following average waste loads based on "100 percent operation":

Table A-2.
Summary of Permit Application Data
July 1971

Parameter	Load	
	kg/day	lb/day
Flow	23,700[a/]	6.26[b/]
BOD	1,120	2,470
COD	4,380	9,650
TDS	7,370	16,250
TSS	73[c/]	160[c/]
Total P	5	10
NH_3-N	23	50

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a/ Flow in m^3/day.
b/ Flow in mgd.
c/ These values were later declared to be in error.

The Company submitted updated flow [Table A-3] and waste load [Table A-4] data on February 23, 1973.

Table A-3.
February 1973 Flow Data

Waste Stream	Flow (m^3/day)	Flow (gpm)
Liquid effluents from the thermal oxidizers	7,090[a]	1,300[a]
Distillates etc. from oil dehydration CG evaporator	350	65
Venturi scrubber on CG evaporator	270[b]	50[b]
Scrubbing effluents from the trash incinerator	980	180
Treated sanitary effluents	110	20
Spent cooling waters and miscellaneous blowdowns	3,900	715
Estimated Total	12,700	2,330[c]

[a] Reported later as 1,090 m^3/day (200 gpm).
[b] Reported in 1974.
[c] 2,330 gpm = 3.36 mgd.

Table A-4.
Summary of February 1973 Load Data

Parameter	February 1973 Loads (mg/l)	February 1973 Loads (kg/day)	February 1973 Loads (lb/day)	Loads at Full Phase I Production Capacity (mg/l)	Loads at Full Phase I Production Capacity (kg/day)	Loads at Full Phase I Production Capacity (lb/day)
BOD	77	980	2,170	81	1,040	2,300
COD	177	2,280	5,030	191	2,590	5,720
TSS	25	310	680	40	540	1,200
Zinc	0.8	9	20	3.0	40	90
Fecal Coliforms	-	-	-	1,500/100 ml (max.)		-

Company Sampling Results

Waste loads observed in the plant effluent (Outfall 001) during 1972, 1973 and January through April of 1974 are summarized in Table A-5. These data, taken from the Company monthly reports to the State of Indiana, indicate that BOD and COD concentrations and loads have decreased steadily from 1972 to the present. Total suspended solids concentrations have remained relatively stable although loads have increased. Chlorides increased significantly from 1972 to 1973 but the chloride concentrations and loads have since continued at more or less the same level. Bromides showed the largest percentage increase of all parameters. Zinc levels have stayed about the same since 1973. Considering the steady increase in Clinton production from 1972 to 1974, it is somewhat surprising that there have not been greater increases in the major parameter waste loads.

The 1972 data were erratic, perhaps indicating early efforts to shake down plant facilities. During the January through April 1974 period, daily BOD, COD and TSS loads averaged about 770, 1,700, and 570 kg (1,700, 3,700 and 1,250 lb), respectively. These loadings were about 70 percent of the design values predicted for full Phase I production. The total suspended solids loads approximated about 70 percent of the BOD loads.

One very striking observation from all the Clinton results is the very low COD to BOD ratio of around 2.0 to 2.5 consistently recorded for Clinton wastewaters. This is undoubtedly due to the unique waste treatment facilities at this location.

The Company for some time has been conducting sampling at selected locations inside the Clinton Laboratories' complex. COD values for the period January 1974 through July 1974 are summarized in Table A-6 for seven internal sampling points. Stations 5 and 6 flows are included in Station 7 data. Adding the COD loads from stations 1, 2, 3, 4 and 7 gives a total COD loading of 1,490 kg (3,284 lb)/day as an average over the period January through July 1974. It is not known if the stripper effluent associated with the Carver-Greenfield system is included in this total. The Outfall 001 loads for the period of January through April 1974 in Table A-5 averaged 1,680 kg (3,703 lb) COD/day. Considering that different time periods are involved for the two sets of data, the COD loads seem to agree fairly well. These loads, representative of Clinton operations over the first part of 1974, were about 65 percent of those predicted under full Phase 1 production capacity. Also from the data in Table A-6, it is evident that the Carver-Greenfield distillate was lower in COD than predicted. Conversely, significant and unaccounted for waste sources were contributing large waste loads at sampling locations 1 and 4, which were reported as representing primarily non-contact cooling water streams. Extraneous waste sources are likely present even through no barometric condensers are utilized in the Clinton plant. Non-contamination is generally evidenced by COD concentrations in the range of 10 mg/l to no more than 20 mg/l. Sampling locations 1 and 4 over the period January through July 1974 demonstrated COD levels of 33 mg/l and 126 mg/l, respectively. Such sources should be identified and controlled and/or eliminated.

TABLE A-5
Summary of Monthly Effluent Waste Loads (Outfall 001)
Eli Lilly and Co., Clinton Laboratories, Clinton, Ind.
Jan. 1972 to Apr. 1974

Parameter	Year					
	1972		1973		1974	
	Average	Range	Average	Range	Average	Range
FLOW						
mgd	3.38	2.90 - 4.90	3.45	2.46 - 4.15	4.34	4.23 - 4.47
m^3/sec	0.148	0.127 - 0.214	0.151	0.108 - 0.181	0.190	0.185 - 0.195
BOD						
mg/l	70	48 - 185	69	43 - 111	48	40 - 53
lb/day	2,390	1,846 - 7,556	1,963	1,326 - 3,018	1,714	1,403 - 1,915
kg/day	1,084	837 - 3,427	890	60 - 1,369	77	636 - 86
COD						
mg/l	196	113 - 421	140	104 - 218	102	80 - 121
lb/day	6,770	4,320 - 17,200	3,980	3,073 - 5,333	3,703	2,835 - 4,007
kg/day	3,071	1,960 - 7,802	1,805	1,394 - 2,419	1,680	1,286 - 1,818
TSS						
mg/l	27	20 - 53	35	21 - 65	34	24 - 55
lb/day	912	501 - 2,126	1,035	520 - 2,040	1,250	806 - 1,990
kg/day	414	227 - 964	70	236 - 925	567	336 - 903
CHLORIDES						
mg/l	72	57 - 143	161	119 - 214	150	104 - 180
lb/day	2,270	2,250 - 3,680	4,660	3,150 - 6,710	5,410	3,760 - 6,480
kg/day	1,030	1,021 - 1,669	2,114	1,429 - 3,044	2,454	1,706 - 2,939
BROMIDES						
mg/l	0.7	0.4 - 1.3	2.4	0.5 - 9.5	10.0	5 - 16
lb/day	25	15 - 50	70	12 - 293	370	185 - 590
kg/day	11	6.8 - 23	32	5.4 - 133	168	83.9 - 268
ZINC						
mg/l	0.5	0.2 - 1.2	0.9	0.4 - 2.3	0.9	0.4 - 1.0
lb/day	14	9 - 29	27	13 - 62	31	16 - 36
kg/day	6.4	4 - 13	12	5.9 - 28	14	7.3 - 16

Table A-6.

COD Values for Sampling Points in Clinton Laboratories
Jan - July, 1974

Sampling Location No.	Description	Estimated Flow (m^3/day)	Estimated Flow (gpm)	COD Range[a/] (mg/l)	COD Average (mg/l)	COD Average (kg/day)	COD Average (lb/day)
1	Non-contact cooling waters from chemical operations and north utility equipment area plus surface runoff from NW quadrant	10,900	2,000	20 - 62	33	360	793[b/]
2	Boiler house blowdowns, south cooling tower waters, plus runoff from central service	270	50	56 - 145	103	28	62
3	Non-contact cooling waters from fermentation with surface runoff from SW quadrant	410	75	9 - 39	15	6	14
4	Non-contact cooling waters from Product Recovery, the east utility equipment area and product recovery strippers plus surface runoff from SE quadrant	1,360	250	83 - 165	126	172	380[b/]
5	Effluent from Smith-Loveless sewage treatment plant	80	15	19 - 55	29	2	5
6	Distillate from Carver-Greenfield evaporator system	220	40	1,492 - 2,452	2,045	446	983
7	Effluents from the two John Zink incinerators, the Bartlett-Snow incinerator, the Carver-Greenfield evaporator, plus storm water from the NE quadrant	3,820	700	183 - 286	242	924	2,036

[a/] Monthly concentration.

[b/] Significant waste loads contained in these flows not previously accounted for by Company.

The Company conducted trace metal analyses on the Outfall 001 effluent on random days during 1973-1974 that yielded the following results:

Table A-7
Summary of 1973-1974 Trace Metal Data

Parameter	Median (mg/l)	Maximum (mg/l)
Copper	<1.0	3.10
Iron	<1.0	<1.0 [a/]
Lead	<0.05	0.26
Mercury	<0.004	<0.004
Aluminum	<0.10	<0.10
Chromium	0.03	0.08

[a/] Concentration of 1.4 mg/l noted during August 1974 EPA-State survey that also showed zinc values of 1.4 to 1.6 mg/l and some 136 kg (300 lb)/day of NH_3-N in the effluent from Outfall 001.

DEVELOPMENT OF NPDES PERMIT CONDITIONS

State Waste Load Limitations

In February 1970, the Company requested the State of Indiana for permission to discharge up to 1,430 kg (3,150 lb)/day BOD based upon a raw load of 180,600 kg (398,200 lb)/day BOD. Appropriate waste treatment was described which would provide a 99.2 percent BOD reduction. Major contributing waste sources were as described in Table A-1. Normally only the watery process wastes, sanitary sewage and untreated clear water stream are expected to contribute waste loads to the treatment facility at most pharmaceutical plants. Equivalent raw waste loads for the Clinton facility are thus estimated to be in the range of 11,300 to 13,600 kg (25,000 to 30,000 lb) BOD/day.

On April 21, 1970, the State gave notice of considering the Company's preliminary plans and specifications and attached certain conditions to the plans. Anticipated wastewater characteristics of the final effluents were 1,137 kg (2,507 lb)/day BOD, 1,157 kg (2,550 lb)/day chlorides, 243 kg (535 lb)/day bromides and 250 kg (550 lb)/day zinc contained in a total flow of 21,200 m^3/day (5.6 mgd). The State also specified that the Carver-Greenfield effluents should receive additional treatment because of the very high organic concentrations in these particular waste streams.

On September 21, 1971, the State of Indiana gave approval to plans and specifications for the Clinton waste treatment facilities. The State apparently accepted the conditions of 1,137 kg (2,507 lb)/day BOD an 34 kg (76 lb)/day TSS to be contained in a total wastewater flow of 15,200 m^3/day (3,97 mgd). The State recommended that the Company design and install adequate facilities for the treatment of the distillates from the Carver-Greenfield operations.

In mid-1972, the State requirements for the single effluent from the Clinton facilities (Outfall 001) were given as: BOD - 1,137 kg (2,507 lb)/day or 53 mg/l maximum; TSS - 40 mg/l maximum; chlorides - 1,157 kg (2,550 lb)/day or 54 mg/l maximum; bromides - 243 kg (535 lb)/day or 11.4 mg/l, and zinc - 1 mg/l.

Rationale for Effluent Limitations

Various factors including a lack of data, the nature of the Clinton facilities and/or perhaps the reluctance of the Company to provide sufficient interpretive information made it difficult to determine an equivalent raw waste load for the Clinton Laboratories. Our best estimates of raw waste load under full Phase I production capacity are 11,300 to 13,600 kg (25,000 to 30,000 lb) BOD/day and 22,700 to 27,200 kg (50,000 to 60,000 lb) COD/day. Treatment performance achieved by the Clinton facilities is currently estimated to be roughly 90 percent for both BOD and COD.

Based upon past data and from all indications given by the Company to the State, Clinton Laboratories up through full Phase I production is more than capable of holding average daily BOD, COD and TSS loads down to 1,137 kg (2,507 lb), 2,310 kg (5,100 lb) and 820 kg (1,800 lb) respectively. Accordingly, average daily immediate load limits in the Clinton permit were established as 1,137 kg (2,507 lb) BOD, 2,310 kg (5,100 lb) COD, and 860 kg (1,900 lb) TSS.

Evaluation of existing waste control, treatment and disposal practices identified several areas where improvements resulting in reduced waste loads could be made. The most significant reduction could be achieved by providing treatment for the waste distillate from the Carver-Greenfield evaporator unit. This small 150 to 230 l/min (40 to 60 gpm) waste stream contributes a substantial waste load because of excessive BOD and COD concentrations calculated at 2350 and 4700 mg/l, respectively, for full Phase I operations. These distillates are readily amenable to additional inexpensive treatment and should be receiving treatment today. It is noted that this same recommendation was made by the State of Indiana on September 21, 1971, when approval was given to the Clinton waste treatment facilities. A minimum requirement of a 62.5 percent BOD reduction and a 50 percent COD reduction was selected for this waste stream. Assuming the addition of a biological treatment unit on the distillate waste stream, it should be possible to reduce full Phase I BOD loads from 1,137 to 658 kg (3,507 to 1,450 lb)/day and COD loads from 2,310 to 1,540 kg (5,100 to 3,400 lb)/day. A corresponding reduction of TSS loads from 800 to 660 kg (1,770 to 1,450 lb)/day should be achievable by addition of the distillate treatment unit. This would be an overall 20 percent reduction.

Although the percentage waste load reductions achieved by treatment of the Carver-Greenfield distillate do not appear particularly outstanding, they are considered sufficent to meet waste treatment requirements for the bulk pharmaceutical plants in the industry. The Clinton facility has been given certain extra credits for achieving exemplary COD reductions. Also, the plant has other alternative means available for reducting waste loadings such as removing or controlling waste streams connected to cooling water discharges.

Recognizing the uncertainties in developing raw waste loads for Clinton and other exigencies, accordingly the permit limits for full Phase I operations on an average daily basis were set at (1,550 lb) BOD, (3,750 lb) COD and (1,525 lb) TSS. These figures result in average waste reductions of around 94.5 percent for BOD and 93.0 percent for COD.

Regarding nitrogen and phosphorous effluent loads, based upon past data, phosphorous would appear to present no problems. Ammonia nitrogen levels in the Clinton effluents are marginal with respect to BPT industry limits. Data provided by the Company in mid-1974 indicated levels of 110 to 200 kg (240 to 450 lb)/day ammonia-N vs. 150 kg (340 lb)/day established in the NPDES permit for Phase I Clinton conditions. However, limited data collected by Eli Lilly in September-October 1974 reports that ammonia-N is now averaging about 290 kg (635 lb)/day. Clinton attributes the higher "recorded" levels of ammonia to better measurement techniques and ammonia resulting from breakdown of raw materials used in reactions, through incineration and other waste processing. Identification of contributing nitrogen souces and possible treatment may be necessary, partially dependent upon a more adequate data base. If ammonia reduction is necessary, first priority should be given to selected waste stream scavenging and direct in-plant recovery means.

Clinton laboratories, over the past 24 months, has apparently reduced zinc levels in the final effluent to less than 1.0 mg/l. Tentative and/or long-term limits hagve been set on trace constituents including phenolics, zinc, iron, lead, copper and sulfates because these elements are indicated to represent possible or probable problems. Load limits for these elements have been based upon an average total effluent flow of 16,428 m^3/day (4.34 mgd) during 1974 and respective concentrations for these parameters of 0.25, 1.0, 1.0, 0.1, 0.5, and 0.5 mg/l.

Phase II load limits were set at twice the Phase I limits. Maximum daily limits for all parameters except fecal coliforms were established as 150 percent of average daily limits. Fecal coliform limits, as a matter of policy, were set at 200 and 400 organisms/100 ml for the average and maximum daily conditions, respectively.

Important dates for the Clinton permit include the date of permit issuance assumed as of around November, 1974; the attainment of full Phase I production expected to occur around mid-1975; and the attainment of full Phase II production expected in late 1976 or early 1977. The expiration of the permit has been set as June 30, 1977. The numerical limitations have been staged to conform to the expansion phases through 1977.

PHARMACEUTICAL INDUSTRY

CASE HISTORY B

ELI LILLY AND CO., INC., TIPPECANOE LABORATORIES
LAFAYETTE, INDIANA

(FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PLANT)

ELI LILLY AND CO., INC., TIPPECANOE LABORATORIES, LAFAYETTE, INDIANA (FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PLANT)

BACKGROUND

The Eli Lilly and Company Tippecanoe Laboratories at Lafayette, Indiana, manufactures bulk pharmaceutical fine chemicals, antibiotics, herbicides, and miscellaneous products using fermentation and synthetic chemical processing technology.

The plant was reported first opened in 1954 as an antibiotics plant, and production was broadened in 1957 to include chemical manufacturing. Since 1957 the Company indicates growth has been extensive, approximating a tenfold increase. In 1972, antibiotics and antibiotic derivatives comprised 50 percent or more of total plant activities. However, by 1974, the ratio of antibiotic production to total plant activities had somewhat decreased. Tippecanoe operations are currently categorized as roughly 40 percent fermentation; 20-30 percent herbicides production; and 30-40 percent production of various organic synthesized drugs and medicinals.

The plant makes in the order of 166 chemical intermediates and 88 finished bulk products. The major products include analgesics, anaesthetics, antibiotics and antibiotic intermediates, antihistamines, barbiturates and barbituric derivatives, alkaloids, mercuric compounds (i.e. merthiolate), antidiabetics, opium derivatives, tranquilizers, the herbicide Treflan or trifluralin, and numerous other chemicals and intermediates. In the last few years, the plant has embarked upon large scale recovery and sale of sulfuric acid. No production figures were obtained for sulfuric acid. A changing product mix undoubtedly has a less than favorable impact upon the industrial waste treatment facilities.

In 1972, essentially three antibiotics were made with erythromycin predominating. Today the Cephalosporin-type antibiotics are largely manufactured with some "Tylan" (an animal antibiotic) and possibly others. The production of trifluralin initiated in the past 3-4 years is now quite significant. All processing is supposedly carried forth by batch methods. Final packaging is primarily done at Eli Lilly's Indianapolis, Indiana plants.

Tippecanoe is operated 24 hours per day, 7 days a week, and has about 1,050 employees. Around May 1974, NFIC-Denver was asked to provide assistance in developing the NPDES permits for Eli Lilly and Company plants at both Lafayette and Clinton, Indiana. The Tippecanoe Laboratories at Lafayette was visited by NFIC-Denver on May 10, 1974, and again on June 26, 1974. The visits provided valuable information on current plant practices.

PROCESSES

The Lafayette plant has four main boilers, three on coal and one on fuel oil. Water supply for the plant, obtained from Company-owned wells, is treated with polyphosphates and chlorinated. The potable water supply is softened by lime treatment and the boiler water receives softening principally by zeolite resins. Wastewaters from the treatment plant are discharged to the sanitary sewer system.

"Treflan," the principal herbicide manufactured, is mainly a pre-emergent crab grass and weed killer utilized for cotton and soybean farming. According to the literature, the main process for synthesizing Treflan consists of nitrification in successive steps with p-chlorobenzotrifluoride, hydrochloric acid, sulfuric acid and fuming nitric acids as raw materials. The p-chlorobenzotrifluoride is converted over to the mononitro intermediate then to the dinitro intermediate, dissolved in chloroform and aminated with soda ash to yield trifluralin. Trifluralin is mixed with aromatic naphtha and emulsifiers to the desired final formulation. Spent acids are reported being recovered. Residual acids, salt water layers, and chemical washwaters together with unrecoverable solvents are discharged to the plant sewers. It is noted that Treflan has a reported toxicity in the range of 14 to 58 ppb expressed as an LC_{50} over 24 hours derived for relatively sensitive fish species.

WASTE TREATMENT AND CONTROL

Waste Treatment in the 1950's

The early waste treatment works, completed in April 1954, are described in a series of papers by Howe and Paradiso in 1956 (63), Howe and DeMoss in 1957 (33), and Paradiso and Howe in 1958 (100).

The early treatment facilities consisted of neutralization, preaeration (later converted to modified activated sludge), biofiltration, settling, anaerobic digestion, nitrification, chlorination and sludge drying. Installation cost was cited in 1954 as $750,000. Wastewater problems were principally high dissolved and colloidal solids, BOD, color, odors, and solvents. Wastes being received into the system included antibiotic wastes consisting mainly of spent fermentation broths and associated effluents, and sanitary waste streams including various equipment and floor washings. Treatment design called for 3,975 m^3/day (1.05 mgd) of mixed wastewaters containing a maximum BOD load of 5,670 kg (12,500 lb)/day.

Spent cooling waters from the Tippecanoe installation amounted to about 15,140 m^3/day (4.0 mgd) and received no treatment. These were merged with the treated antibiotic and sanitary wastewaters prior to final discharge to the Wabash River. It was anticipated that the sanitary wastes and spent antibiotic broths, 290 m^3/day (77,000 gpd); floor washings, 230 m^3/day (60,000 gpd); and wash waters, 720 m^3/day (190,000 gpd) would have the following waste loads:

	Flow		BOD		Total Solids		TSS	
	(m^3/day)	(gpd)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)
Min. flow	510	135,000	860	1,900	1960	4330	61	135
Avg. flow	1,240	327,000	3,240	7,140	9330	20,560	240	530
Max. flow	1,990	525,000	3,360	7,400	7640	16,850	236	520

Howe (6) describes the installation in the mid-1950's as having biological treatment and chlorination of antibiotic wastewaters. The biological treatment system employed both turbine aeration and diffused air, and had the following characteristics:

Parameter	Antibiotic Wastes Influent	Treated Effluent
BOD	25,000 mg/l	75 mg/l
TS	35,000 mg/l	580 mg/l
pH	3.9	7.5

There were two aeration basins, 17m x 6m x 5m (56 ft x 20 ft x 16 ft) having a mixed liquor solids level averaging 3000 mg/l. The basins used about 17.2 m^3 of air/kg (275 scf air/lb) of BOD removed. The BOD loadings were 7.2 to 9.6 kg/day/m^3 (450-600 lb/day/1,000 ft^3) of aeration basin capacity (33, 63, 100). Equipment and floor washings, sanitary wastes, cafeteria and laboratory wastes were combined into a single stream that received pre-chlorination and passed through a comminutor before discharge into the settler that followed the aeration basins. The combined wastes passed to a second treatment system consisting of high-rate trickling filters each 23 m (76 ft) in diameter by 1.5 m (5 ft) deep operating in parallel with the effluents going to a secondary clarifier. Final clarifier overflows received post-chlorination before combining with the cooling waters and discharging to the River. Howe and Paradiso (63) in 1956 reported that the final effluent from the treatment system after combining with the cooling water stream had an average BOD of 12.2 mg/l (equivalent to approximately 230 kg (500 lb)/day BOD discharged); a pH of 7.0 to 7.4; a total solids level of 380 to 410 mg/l; and no evidence of color, odor or toxicity. The clarifier sludges went to single or double-stage anaerobic digestors, were dried and used as a soil conditioner.

Digester supernatants went to a nitrification basin 8.8 m x 1.5 m x 3.8 m deep (29 ft x 5 ft x 12.5 ft deep), equipped with auxiliary aeration. These nitrified supernatants were first routed to the trickling filters but later diverted to the "primary" clarifier.

The 1956 Eli Lilly report (63) cites the availability at that time of vacuum filtration equipment for handling waste sludges, solvent recovery operations, and evaporators for the recovery of spent broth. It is not known whether the spent broth evaporators were ever put into use.

When the treatment facilities went into operation, it was soon found that real operating conditions were much different than what had been assumed under the original treatment plant design criteria. Actual waste loads were tremendously higher than the design criteria as shown:

Parameters	Unit	Design Loads		Actual Loads	
		(kg/day)	(lb/day)	(kg/day)	(lb/day)
BOD	Clarifiers	240	530	2,720-5,440	6,000-12,000
	Trickling filters			910-1,810	2,000-4,000
TSS	Clarifiers	3,450	7,600	5,440-10,880	12,000-24,000
	Trickling filters	2,950	6,500	4,540-9080	10,000-20,000
Sludge	Digester	38[a]	10,000[b]	151	40,000[b]

[a] Volume in m^3/day.

[b] Volume in gpd; 5 percent solids content assumed.

Typical performance results of the treatment system given by Eli Lilly in 1958 are shown in Table B-1. The data indicated the Tippecanoe treatment facility was giving waste removals of 89.9 to 92.4 percent for BOD and 90.5 to 92.4 percent for TSS.

Howe and DeMoss (33) cite serious corrosion problems through the 1950's because of the nature of the wastes being handled. Odors were also a pervading problem but various approaches considered successful were:

1) Quick removal of odor-producing solids from the biological oxidation processes.
2) Adequate oxidation of organic matter with sufficient air.
3) Addition of odor-suppressant chemicals.
4) Control of odor-producing vapors by water mists.
5) Evaporation of spent broths.
6) Use of oxidizing chemicals such as chlorine-containing agents.
7) Complete digestion of solids.
8) Complete combustion of sludge gases.
9) Close control of treatment processes.

Table B-1
Characteristics of Wastewaters Treated Around 1957-1958
Eli Lilly & Co., Tippecanoe Laboratories, Lafayette, Ind.

Source	Temperature		pH	BOD		Total Solids		TSS		TDS	
	°C	°F		(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)
Antibiotic Waste Neutralization Tank (A) Influent	49	120	3-5	8,620	19,000	9,660	21,300	5,440	12,000	4,220	9,300
Tank (A) Effluent to Antibiotic Waste Holding Tank (B)	49	120	7	8,620	19,000	9,660	21,300	5,440	12,000	4,220	9,300
Tank (B) Effluent											
to Aeration Tank (C)	32	90	6.0	4,310	9,500	4,830	10,650	2,720	6,000	2,110	4,650
to Digesters	32	90	6.0	4,310	9,500	4,830	10,650	2,720	6,000	2,110	4,650
Sanitary Wastes to Aeration Tank (C)	18-71	65-160	2.3-13	363	800	725	1,600	499	1,100	227	500
Secondary Clarifier	10-24	50-75	7.2	680	1,500	1,130	2,500	570	1,250	570	1,250
Final Effluent leaving chlorine contact Chamber	24-29	75-85	7.3	680-910	1,500-2,000	1,130	2,000	454	1,000	454	1,000

Waste Treatment in the 1960's

Howe in 1962 (21) described various waste streams originating from antibiotics production as:

1) Liquid and solid wastes directly from fermentation processes (high strength);
2) Liquid wastes from extraction and purification processes (high strength);
3) Liquid and solid wastes from recovery processes (high strength);
4) Washings of equipment and floors (varying strength);
5) Spent cooling waters;
6) Laboratory wastes, sanitary sewage and miscellaneous (varying strengths).

He characterized these wastes as having an irregular flow pattern, a continuously-changing waste composition, high dissolved and colloidal solids, fluctuating pH, high BOD, temperature, toxicity, color and odor.

Changes in the waste treatment facilities during the mid-1950's and early 1960's basically consisted of the addition of a third-stage biological treatment step: activated sludge following the high-rate trickling filters. The high-rate trickling filter effluents were returned to the primary clarifiers, thence through the chlorine contact chamber and the third-stage biological treatment sub-system before final discharge to the river. The third stage of biological treatment was reported to consist of a 378 m^3 (100,000 gal.) clarifier and a shallow 1.8 m (6 ft) deep aeration basin of 3,400 m^3 (900,000 gal.) capacity.

The clarifier following third-stage activated sludge was under construction in early 1962. At that time, chemical wastes, presumably from organic synthesis, were observed as being present in the waste treatment circuit. The chemical wastes were being introduced into the (aerated) nitrification tank, prior to the primary settlers and the second-stage biological trickling filters.

Waste characteristics of the waste treatment facility influent in the early 1960's are shown in Table B-2.

High-rate two-stage aeration comprising the first stage of biological treatment was reported as giving 80 percent BOD reduction of the strong antibiotic fermentation wastes. The MLSS concentration in this sub-system was maintained around 6,000 to 8,000 mg/l. The high rate trickling filter sub-system constituting the second stage of biological treatment and receiving the treated first-stage antibiotic wastes plus equipment and floor washings and chemical wastes, was reported as receiving BOD loads of 5,260 to 9,980 kg (11,600 to 22,000 lb)/day and providing 70 to 80 percent BOD reduction. The BOD removal within the third stage system was reported averaging about 50 percent. Overall treatment plant BOD removal efficiency was rated by Howe as between 90 and 95

Table B-2

Characteristics of Wastewater Entering Treatment System in Early 1960's (21)
Eli Lilly & Co., Tippecanoe Laboratories, Lafayette, Ind.

Wastewater	Flow		BOD			Total Solids			Suspended and Colloidal Solids				Color	Temperature	
	(m^3/day	(gpd)	(mg/l)	(lb/day)	(kg/day)	(mg/l)	(lb/day)	(kg/day)	(mg/l)	(lb/day)	(kg/day)	pH	(Co-Pt)	°C	°F
Antibiotic Liquid Wastes	568	150,000 average	15,000-35,000	18,000-40,000	8160-18,100	20,000-50,000	25,000-63,000	11,300-13,000	10,000-40,000	15,000-40,000	6800-18,100	3-10.5	20,000-30,000	43.3-48.9	110-120
Equipment and Floor Washings and Sanitary Wastes	378-1510	100,000-400,000	2,000-8,000	4,000-16,000	1810-7260	3,000-15,000	6,100-31,000	2,770-14,100	2,000-9,000	4,000-18,200	1810-8,300	2.0-11.5	1,000-5,000	12.8-29.4	55-85
Total Wastes	946-1510	250,000-400,000		22,000-56,000	9980-25,400		31,100-94,000	14,100-42,600		19,000-58,200	8620-26,400				

percent. Ammonia content in the final effluents was 4.3 mg/l. Comparing waste loads of 1961 (21) with those of the 1950's at Tippecanoe, the important conclusion may be drawn that raw waste loads more than doubled over the intervening 5 to 7 years, while expansion in the waste treatment works was far less significant.

Howe (21) cites special studies conducted by Eli Lilly towards improving waste removal efficiencies and other investigations on the toxicity of certain antibiotics to biological treatment. Some antibiotics even if present at very low concentrations, are toxic to the microflora in the aeration system and can quickly render the entire system static. Even though the microflora may be acclimated to the presence of one antibiotic at a certain concentration, it may fail completely when another antibiotic is added to the system. Howe recommends that certain antibiotic wastes should be diluted to ensure successful biological treatment. This is best accomplished in large aeration tanks that can accommodate high hydraulic and BOD loadings.

Sludge Centrifuging, Late 1960's and Early 1970's

A 1972 report (52) describes sludge centrifuging within the waste treatment installation. After activated sludge treatment, spent antibiotic wastes are settled in a series of clarifiers and thickeners. The settled sludges are pumped to a Pennwalt Sharples P-5400 centrifuge. Supernatants are returned to the waste treatment plant, while sludge solids are pumped into a truck and hauled away. The centrifuge receives 265 to 568 l/min (70 to 150 gpm) of sludge liquors with a solids content of 3 to 6 percent. The outflows consist of a centrate having no more than 0.8 percent solids and a readily-handled sludge concentrate of 20 to 30 percent solids, amenable to incineration. The centrifuge system is reported as having reduced sludge truck hauling needs by as much as 80 percent. The 363 kg (800 lb)/minute of sludge previously generated were reduced to about 75 kg (166 lb)/minute. Sludge volume was reduced from 0.35 to 0.07 m^3 (12.5 to 2.5 ft^3)/minute.

Similarly, the synthetic chemical wastes are neutralized and settled, with the underflows going to centrifuges. The partially-treated chemical waste overflows from the settlers are combined with the effluents from the antibiotics-sanitary waste treatment systems. The combined flows receive final settling in two clarifiers before discharge to the River.

The centrifuge sub-system was installed in 1970. Antibiotic sludges were admixed with relatively small quantities of Nalco polyelectrolytes (0 to 11 l/min (0-3 gpm) of 0.02 percent Nalco No. 610 solution). Nothing was added to the chemical waste sludges. The Tippecanoe plant as of 1974 had two centrifuge units in operation.

Odor Abatement, Late 1960's, Early 1970's

Around 1967, the Company covered the aeration tanks in its first stage of biological treatment. The centrifuge operations were also enclosed within a separate building. Odors from these processes were carried in a 1.5 m (5 ft) ducting system to an incinerator put into operation around this time. In 1970, the Company converted the two high-rate trickling filters previously available into aeration tanks, and gave them dome-type coverings to contain the noxious odors and eventually carry them to incineration. In order to supplement the single incinerator, the Company attempted to duct the collected noxious air streams into the fire boxes at its main power plant. However, because of the large volumes of air being carried and secondary odors being created, they found it necessary to install two more incinerators, burning natural gas on an interruptable schedule. Low sulphur fuel oil is used as standby. The incinerator off-gases are water scrubbed with effluents discharged to the liquid waste system. Eli Lilly, as of 1973, reported that more than $2 million had been invested in odor abatement equipment, and fuel bills for the three incinerators were running about $13,000 monthly (49). The present air ducting system also vents various fermentation buildings and some of the more critical chemical process sectors. As of early 1974, the Company fully covered one of the two aerated lagoons within the chemical waste treatment system and the second lagoon was being enclosed as of around June, 1974.

Existing Waste Treatment and Control Systems

The Tippecanoe treatment works handle waste waters from the fermentation area separate from the chemical wastes coming from general chemical manufacturing. The overall works include more or less three separate waste collection and treatment systems: 1) the spent fermentation antibiotics broth; 2) sanitary wastes, floor and equipment washings and miscellaneous; and 3) mixed chemical waste waters.

The fermentation wastewaters enter the "100 System." This treatment system consists of waste holding; settling, 378 m^3 (100,000 gallon) capacity; "pre-aeration" in four activated sludge basins 1,700 m^3 (450,000 gallon) capacity apparently in parallel; and two sludge thickening tanks. Thickened sludges are sent to the centrifuge building. Daily flows being received into this system in mid-1974 were averaging 946 to 1,140 m^3/day (250,000 to 300,000 gpd), or 43 to 72 percent over the system design flow of 662 m^3/day (175,000 gpd). New additions were planned to the fermentation treatment system by the Company, probably during the latter half of 1974, but the new criteria appear to be less desirable than original design objectives. Manufacturing change and expansion seem to be occurring much faster than the capability of the treatment facilities to handle such changes. Overflows leaving the "100" Treatment System are directed to second-stage biological treatment.

Sanitary sewage, equipment and floor washings, washwater from the mycelia storage bins, backwashes from the water treatment system and miscellaneous streams enter the "200 System." In this system, the appropriate waste streams, after passing through a comminutor, join with the fermentation overflows from the sludge thickening tanks and these combined streams enter "primary clarifiers" in parallel followed by two aeration tanks in parallel. Sludges from the 200 System primary clarifiers are sent to the centrifuge building or carted away to landfill. The aeration basin effluent combines with effluent from the "300 system" and enters two "final clarifiers" before eventual discharge. These final clarifiers were observed to be significantly overloaded especially with respect to TSS removal.

The somewhat independent treatment system for chemical wastewaters including those from trifluralin manufacturing is described as the "300 System." The system is a series of basins installed at various intervals since 1954. Chemical wastewaters enter a holding chamber, overflow to a clarifier, then flow to a box where lime is added for neutralization, a second clarifier, an aerated chamber followed by another aerated chamber and then an aerated basin, with the overflows then going into another clarifier and a pump pit. From the pump pit, the chemical waste flows enter two "activated sludge" aeration basins or lagoons operated in series. Waste detention time is reported to be 1.0 to 1.4 days. Unfortunately, the chemical waste treatment system has ample opportunities for bypassing and some of these bypassed streams can possibly enter the untreated cooling water drainage into Outfall 001. The chemical waste treatment system is presently utilizing a full-scale but experimental carbon absorption facility, mainly for the removal of color from the Treflan wastewaters. These particular wastes resulting from nitrification have an intense yellowish-orange color which is not adequately reduced through biological treatment.

Other important aspects of the waste treatment and control works include the sludge centrifuge building housing a pair of Sharples centrifuges, a centralized solvent recovery sector, extensive air ducting systems for collecting and carrying noxious odors from select processing and treatment sectors to three different incinerator units on site, and a John Zink thermal oxidizer used for burning concentrated liquid and solid wastes. The John Zink and the other three incinerators are equipped with water scrubbing devices which in turn return some organic loads to the liquid waste collection system.

Selected concentrated wastes having strengths of a few thousand mg/l of BOD and COD as reported by the Company are stored within six 116 m^3 (30,000 gal.) tanks built into the side of the hill next to the John Zink thermal oxidation unit. The wastes are eventually incinerated in the John Zink system. The scrubber effluents from the John Zink together with surface drainage from around the incinerator unit and associated waste storage tanks appear to flow directly into the Outfall 001 and then to the Wabash River.

Mycelium separated from fermentation broths is collected, dried and mixed with animal feeds or otherwise prepared as a pre-mix feed. Mycelium not incorporated into feed supplements is carted away to landfill. In the recovery area, mycelium is stored in a "live bottom bin" prior to going to the dryer. The storage bin is periodically cleaned with liquids bled to the sanitary waste ("200") system.

The combined treated fermentation, sanitary, chemical and miscellaneous wastes leaving the final clarifiers from the 100, 200 and 300 waste treatment systems are merged with untreated spent cooling waters in Outfall 001 that discharges to the Wabash River. The cooling waters in this sewer have been reported by the Company as uncontaminated, originating from condensers and cooling jackets in the plant. Outfall 001 also captures barometric condenser discharges, and bottoms from a distillation column contributing 760 to 1140 m^3/day (200,000 to 300,000 gpd), in addition to scrubber effluents from the John Zink incinerator contributing 2,270 l/min (600 gpm). Accompanying data will show these cooling waters often have greater wasteloads than are contained in the (100, 200 and 300) treatment plant effluents. This constitutes a large part of the existing problems at Tippecanoe. Flows from the 100, 200 and 300 waste treatment systems total approximately 3,780 to 5,300 m^3/day (1.0 to 1.4 mgd), while Outfall 001 has about 30,300 to 45,400 m^3/day (8.0 to 12.0 mgd) of final wastewaters.

Outfall 002 serves the west side of the main factory grounds. This outfall is reported to contain mainly cooling waters from the jacketing of vessels manufacturing herbicides plus barometric condenser waters from units manufacturing medicinal drugs. This flow, averaging 3,780 to 7,560 m^3/day (1-2.0 mgd), receives no treatment except for a small retention pond close to the River. The Company recognizes some process contamination coming from barometric condensers together with acidity in this discharge. In October 1972, Outfall 002 was the site of a watery solvent spill, the materials lost at that time comprising tetrahydrofuran and diethylanaline from the herbicide manufacturing sector.

Outfall 003 is a relatively new outfall receiving hillside drainage from some 80-120 ha (200-300 acres) of land previously used for waste disposal on top of the promontory overlooking the Wabash River. This drainage is now reaching the River via diverse channels downstream of the main plant, apparently spreading over about one mile of river frontage. Approximately one-half of the drainage is being collected by the Company and routed through the levee in a single flow to the River. This portion of the drainage is Outfall 003. The remainder of the hillside drainage joins with Outfalls 001 and 002 or reaches the River via other means. Total drainage is estimated in the range of 189-757 m^3/day (50,000 to 200,000 gpd). The NPDES permit calls for collecting and bringing this entire drainage back to the main treatment works by 1977 at which time Outfall 003 and other similar drainage will be discontinued.

The Company currently has no chlorination facilities either for the separate treatment plant effluents, or for the 001, 002 and 003 effluents.

Lilly has been experiencing difficulty in disposing of concentrated solid wastes. In Spring, 1974, the Company requested permission of the State to dispose of selected waste materials to public sanitary landfill, but permission could not be secured because of previous leaching problems at the landfill site. The wastes were of four general types:

1) Residues, principally "still bottoms," from distillation-purification operations. Materials ranged from glossy solids to viscous tars.
2) Filter cakes.
3) Organic compounds - including materials not meeting quality specifications for sale.
4) Filter papers - composed of glass, rayon or paper fabric materials, and discarded chemical compounds.

The various waste materials, stored in metal drums, consisted of filter cake from formylglycine, thiophene press papers, off-spec alpha-methyl homoveratryl amine and homoveratric acid, and various waste residues resulting from 2-(3 Phenoxyphenyl) propionitrile, "Papaverine," ethyl malonic ester, isoamyl malonic ester, phenoxyacetophenone, cyclopentamine, dichlorobenzene and dioxyline phosphate.

WASTE LOADS

Waste Loads 1958-1971

The 1958 report by Eli Lilly (100) cited raw waste loads at Tippecanoe of around 9,070 kg (20,000 lb) BOD/day, TSS of 5,900 kg (13,000 lb)/day and TDS of 10,400 kg (23,000 lb)/day. Waste removals were given as 83-91 percent for BOD and 86-92 percent for TSS. A 1962 report by Lilly (21) described total waste flows approaching 946 to 1,510 m^3/day (250,000 to 400,000 gpd) containing daily BOD loads of 9,980 to 25,400 kg (22,000 to 56,000 lb)/day and total solids of 14,100-42,700 kg (31,000 to 94,000) lb/day. Information sheets provided by the Company to the State in March 1969 stated that BOD loads into the treatment system at that time were running 5,700-19,300 kg (12,600 to 42,500 lb)/day, but future loads could be expected in the range of 18,100-22,700 kg (40,000 to 50,000 lb)/day. The final effluents to the River were said to approximate a total of 22,700 m^3/day (6 mgd) containing 47-50 mg/l BOD and 25-50 mg/l TSS. These latter figures likely constituted the prime basis for the State's allowable discharge limits of 1,430 kg (3,150 lb) BOD/day and 544 kg (1,200 lb) TSS/day approved on September 21, 1971. The State specified that if these limits were exceeded, additional treatment would be necessary. Over the past few years, Tippecanoe Labs has consistently exceeded these limits.

In December 1971, the State informed the USEPA that Lilly's new waste treatment facilities being installed at Tippecanoe would have a final plant flow of 34,200 m^3/day (9.03 mgd) and achieve 95 percent BOD reduction, producing by May 1972 an effluent containing 42 mg/l BOD or 1,430 kg (3,150 lb) BOD/day, down from the 5,850 kg (12,900 lb) then being discharged. The EPA gave temporary assent to these load limits but mentaioned that other undesirable waste constitutents were also present in the final effluents including cyanides, mercury, phenolics, chlorinated hydrocarbons and pesticides.

Present Waste Loads

The Company in mid-1974 provided the State and the EPA with a summary of monthly waste load inputs to the waste treatment works for the period of May 1973 through April 1974. In terms of BOD raw waste loads, these tentative figures showed 7120 kg (15,700 lb)/day originating from the antibiotics spent broth sector; 2490 kg (5,500 lb)/day described as sanitary and floor wash raw loads; and 10,000 kg (22,100 lb)/day attributable to chemical process wastewaters. These raw loads averaged 19,700 kg (43,500 lb) BOD/day but monthly values were reported as high as 27,600 kg (60,900 lb)/day.

A recent accounting of raw waste loads was made from detailed Company sampling and analysis sheets on the individual 100, 200 and 300 waste treatment systems for the separate months of March and May, 1974. March 1974 was reported as one of the highest months during 1973-1974 in terms of raw and final waste loads at the Tippecanoe treatment works. Combined treatment plant flows for March through May, 1974, varied on a monthly basis between 3600 and 4430 m^3/day (0.95 and 1.17 mgd), averaging 3970 m^3/day (1.05 mgd). Calculations by NFIC-Denver, based upon this data, show total plant raw waste loads as well as waste removal efficiencies within each of the three treatment systems in Table B-3. The antibiotics fermentation sector was estimated to contribute approximately 40 percent of BOD, TSS and COD plant waste loads. The average of the total plant raw waste loads for the two selected months in 1974 were 24,500 kg (54,000 lb) BOD/day, 44,400 kg (97,800 lb) COD/day, 87,700 kg (193,400 lb) TDS/day, and 5760 kg (12,700 lb) TSS/day.

The results in Table B-3 demonstrate that current treatment reductions are lower than the values previously reported by the Company. The treatment systems appear to lack sufficient capacity and flexibility for coping with current waste loads. On a number of occasions, the State has raised questions as to the sludge handling and TSS removal capabilities of the existing systems. The waste performance data show, in particular, the highly inadequate TSS removals being experienced.

Table B-3

Treatment Plant Raw Waste Loads and Removal Efficiencies
Eli Lilly & Co., Tippicanoe Laboratories, Lafayette, Ind.
March and May, 1974

Parameter	Total Plant Raw Waste Loads		Percent Removals			
	(kg/day)	(lb/day)	Antibiotic "100" Treatment System	Sanitary + Misc. "200" Treatment System	Chemical "300" Treatment System	Overall Treatment Systems*
				March, 1974		
BOD	28,300	62,300	78	[Incr.]	72	71.8
COD	50,300	111,000	59	[Incr.]	72	64.8
TSS	6,300	13,900	[173% Incr.]	[Incr.]	70	51.8
TDS	98,900	218,100	42	[Incr.]	33	28.2
				May, 1974		
BOD	20,400	44,300	77	[Incr.)	80	80.0
COD	38,300	84,500	60	[Incr.]	67	68.0
TSS	5,200	11,500	[280% Incr.]	[Incr.]	59	19.9
TDS	76,500	168,700	34	[Incr.]	22	21.6
Flow Range			795 - 1,135 m^3/day (0.21 - 0.30 mgd)	1,325 - 2,271 m^3/day (0.35 - 0.60 mgd)	946 - 1,514 m^3/day (0.25 - 0.40 mgd)	3,407 - 4,540 m^3/day + (0.90 - 1.20 mgd +)

* Includes raw waste loads for cooling waters in Outfall 001 plus loads for Outfalls 002 and 003.

In October 1974, Eli Lilly presented the USEPA with a new set of raw waste loads for Tippecanoe Laboratories in terms of the maximum operating month:

Source	BOD		COD	
	(kg/day)	(lb/day)	(kg/day)	(lb/day)
Fermentation wastes	10,400	23,000	15,900	35,000
Sanitary and dilute process wastes	2,450	5,400	5,900	13,000
Chemical wastes	14,100	31,100	33,100	73,000
Secondary feed to John Zink unit	3,810	8,400	9,530	21,000
Spent cooling and condenser waters	540	1,200	770	1,700
Hillside drainage	950	2,100	1,450	3,200
Total	32,300	71,200	66,600	146,900

In November 1974, total raw waste loads assumed for the Lilly, Lafayette NPDES discharge permit were raised by the EPA from 24,500 to 30,200 kg (54,000 to 66,500 lb) BOD/day, and from 49,900 to 54,700 (110,000 to 120,500 lb) COD/day.

A summary of monthly effluent values were derived from Lilly, Lafayette's Monthly Report Sheets to the State. These loads applicable to Outfalls 001 and 002 for the period of January 1973 through April 1974 are presented in Tables B-4, 5 and 6. The information shows that waste loads in the combined treated effluents plus cooling water discharges to the Wabash River have significantly exceeded the State limits approved on September 21, 1971, for all months from January 1973 to April 1974. Over this 16-month period, BOD loads averaged 5,000 kg (11,100 lb)/day, with maximum and minimum months of 8,030 kg (17,700 lb)/day and 2,900 kg (6,400 lb)/day respectively. The minimum month loading was about twice the State-stipulated limits for BOD and three times the limitation for TSS.

The combined effluents from the three Tippecanoe treatment systems (100, 200, and 300), which discharge into Outfall 001 were previously cited as averaging about 3,970 m^3/day (1.05 mgd). Considerable spent cooling waters plus miscellaneous streams cause an increase in the Outfall 001 flow up to 30,800 to 40,500 m^3/day (8.4 to 10.7 mgd) as illustrated by Table B-4. Comparing these cooling waters vs. treatment plant effluents for May 1974, it was found that the spent cooling water sewer contributed 17 to 48 percent of the waste discharge loads within Outfall 001. For March 1974, the cooling water sewer contributed 33

Table B-4

Plant Waste Loads (Outfall 001)
Eli Lilly and Co., Tippecanoe Laboratories, Lafayette, Ind.
January 1973 - April 1974

Month	Flow		COD		BOD		TDS		TSS	
	(m^3/day)	(mgd)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)
Jan. 1973	40,700	10.74	12,100	26,700	6,580	14,500	55,500	122,400	3,450	7,600
Feb.	35,200	9.30	14,700	32,500	5,400	11,900	61,100	134,800	2,450	5,400
Mar.	31,800	8.41	13,100	28,800	4,670	10,300	48,300	106,500	2,090	4,600
Apr.	36,000	9.50	14,700	32,300	5,400	11,900	52,900	116,600	2,900	6,400
May	33,900	8.96	15,000	33,000	6,080	13,400	54,100	119,300	3,190	7,030
June	36,600	9.67	11,100	24,400	2,990	6,600	57,200	126,200	2,770	6,100
July	37,000	9.78	10,800	23,700	2,590	5,700	51,600	113,700	4,720	10,400
Aug.	37,200	9.82	12,000	26,400	3,180	7,000	53,000	116,800	5,800	12,800
Sept.	36,300	9.60	10,500	23,200	2,810	6,200	49,000	108,000	6,260	13,800
Oct.	37,800	9.99	11,200	24,800	3,810	8,400	50,300	110,800	4,170	9,200
Nov.	37,200	9.83	10,400	22,900	3,720	8,200	51,100	112,700	1,680	3,700
Dec.	34,000	8.98	15,300	33,800	6,580	14,500	50,500	111,400	2,220	4,900
Jan. 1974	36,900	9.75	16,400	36,100	5,850	12,900	56,200	123,900	3,760	8,300
Feb.	35,100	9.27	18,000	39,600	7,760	17,100	61,100	134,700	2,360	5,200
Mar.	35,500	9.38	17,100	37,700	6,460	14,250	64,000	141,200	2,770	6,100
Apr.	37,700	9.95	10,300	22,700	3,040	6,700	58,300	128,600	3,270	7,200
Avg. 16 mos Data	36,200	9.56	13,300	29,300	4,810	10,600	54,700	120,500	3,370	7,420

Table B-5
Plant Waste Loads (Outfall 002)
Eli Lilly & Co., Tippecanoe Laboratories, Lafayette, Ind.
January 1973 - April 1974

Month	Flow		COD		BOD		TDS		TSS	
	(m^3/day)	(mgd)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)
Jan. 1973	4,160	1.10	118	260	41	90	2,090	4,600	54	120
Feb.	5,450	1.44	154	340	50	110	2,630	5,800	50	110
Mar.	5,720	1.51	399	880	218	480	3,760	8,300	109	240
Apr.	6,060	1.60	490	1,080	290	640	2,900	6,400	95	210
May	5,110	1.35	363	800	236	520	2,590	5,700	82	180
June	6,090	1.61	744	1,640	472	1,040	3,490	7,700	154	340
July	7,760	2.05	513	1,130	295	650	3,950	8,700	122	270
Aug.	6,700	1.77	449	990	236	520	4,080	9,000	141	310
Sept.	6,320	1.67	884	1,950	317	700	3,040	6,700	95	210
Oct.	6,060	1.60	590	1,300	240	530	3,360	7,400	68	150
Nov.	5,110	1.35	190	420	77	170	2,950	6,500	50	110
Dec.	3,290	0.87	118	260	50	110	1,860	4,100	45	100
Jan. 1974	5,450	1.44	680	1,500	313	690	2,720	6,000	109	240
Feb.	5,720	1.51	431	950	263	580	3,520	7,760	109	240
Mar.	5,070	1.34	240	530	141	310	2,180	4,800	73	160
Apr.	6,210	1.64	313	690	171	380	6,170	13,600	95	210
Avg. 16 mos Data	5,640	1.49	408	900	213	470	3,220	7,100	91	200

Table B-6
Plant Waste Loads (Sum of Outfall 001 and 002)
Eli Lilly & Co., Tippecanoe Laboratories, Lafayette, Ind.
January 1973 - April 1974

Month	Flow		COD		BOD		TDS		TSS	
	(m^3/day)	(mgd)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)
Jan. 1973	44,800	11.84	12,200	27,000	6,620	14,600	57,600	127,000	3,490	7,700
Feb.	40,700	10.74	14,900	32,800	5,440	12,000	63,800	140,600	2,490	5,500
Mar.	37,600	9.92	13,500	29,700	4,900	10,800	52,100	114,800	2,180	4,800
Apr.	42,000	11.10	15,200	33,400	5,720	12,600	55,800	123,000	2,990	6,600
May	39,000	10.31	15,300	33,800	6,300	13,900	56,700	125,000	3,270	7,200
June	42,700	11.28	11,800	26,000	3,450	7,600	60,700	133,900	2,900	6,400
July	44,800	11.83	11,200	24,800	2,900	6,400	55,500	122,400	4,850	10,700
Aug.	43,900	11.59	12,400	27,400	3,400	7,500	57,100	125,800	5,940	13,100
Sept.	42,700	11.27	11,400	25,200	3,130	6,900	52,000	114,700	6,350	14,000
Oct.	43,900	11.59	11,800	26,100	4,040	8,900	53,600	118,200	4,260	9,400
Nov.	42,300	11.18	10,600	23,300	3,810	8,400	54,100	119,200	1,720	3,800
Dec.	37,300	9.85	15,500	34,100	6,620	14,600	52,400	115,500	2,270	5,000
Jan. 1974	42,400	11.19	17,100	37,600	6,170	13,600	59,000	130,000	3,860	8,500
Feb.	40,800	10.78	18,400	40,600	8,030	17,700	64,600	142,500	2,450	5,400
Mar.	40,600	10.72	17,300	38,200	6,620	14,600	66,200	146,000	2,860	6,300
Apr.	43,900	11.59	10,600	23,400	3,220	7,100	64,500	142,200	3,360	7,400
Avg. 16 mos Data	41,800	11.05	13,700	30,200	5,030	11,100	57,900	127,600	3,450	7,600

to 70 percent of the total waste loads being conveyed by Outfall 001 to the River. In March 1974, the effluent loads were 6,490 kg (14,300 lb) BOD/day and 2,770 kg (6,100 lb) TSS/day, which were about five times greater than the State limits of September 21, 1971. Besides less than desirable waste removal efficiencies by the treatment facilities, a large portion of the final waste loads is due to the untreated cooling water streams. These "undefined" waste sources should be eliminated or controlled at the earliest possible time.

Monthly values on ammonia nitrogen loadings covering the period January through June 1974 were provided by the Company (Table B-7). The data clearly shows that the large majority of unoxidized nitrogen is associated with the chemical wastewaters within the "300" Sector. Chemical wastewaters contained ammonia concentrations varying from 840 to 1,130 mg/l, equivalent to an average loading of 1090 kg (2,400 lb)/day. Outfall 001 receiving combined effluents from the 100, 200 and 300 treatment systems plus large amounts of spent cooling waters had an average ammonia load of 1,720 kg (3,800 lb)/day. The total ammonia loads to the Wabash River originating from all three Tippecanoe outfalls (001, 002 and 003) averaged about 1,810 kg (4,000 lb)/day. In comparison with this 1974 data, the discharge permit applications of April 1972 and May 1974 showed considerably less ammonia-N: 508 kg (1,120 lb)/day and 1,102 kg (2,430 lb)/day, respectively, for Outfall 001. The EPA survey of September 1973 found 658 kg (1,450 lb)/day ammonia-N, and the State-EPA survey of August 1974 illustrated 1,430 (3,150 lb)/day for Outfall 001.

Outfall 002 was discharging 3,785 to 7,950 m^3/day (1.0 to 2.1 mgd) (Table B-5) of contaminated cooling waters as indicated by monthly BOD loads ranging from 41 to 517 kg (90 to 1,140 lb)/day and averaging 213 kg (470 lb)/day. As high as 884 kg (1,950 lb)/day of COD was discharged with the peak recorded in September 1973.

Outfall 003 represents underground waste percolation and drainage intercepting the surface strata and finding its way to the Wabash River. Total drainage is in the range of 189 to 568 m^3/day (50,000 to 150,000 gpd), or possibly greater. Company data of July 1974, and an EPA-State Survey in August 1974, showed the following characteristics for this outfall:

Table B-7

Ammonia Nitrogen Loadings
Eli Lilly & Co., Tippecanoe Laboratories, Lafayette, Ind.
January - June, 1974

Waste Stream		Concentrations (mg/1)	Loads (kg/day)	Loads (1b/day)
Influent to "100 System"	Average	--	159-381	350-840
	Range	110-470	91-544	200-1,200
Influent to "200 System"	Average	37	68	150
	Range	27-52	41-109	90-240
Influent to "300 System"	Average	970	1,089	2,400
	Range	840-1,130	798-1,393	1,760-3,070
Effluent from "300 System	Average	--		
	Range	390-1,180		
Combined Effluent "100, 200, 300 Systems"	Average	280		
	Range	240-350		
Outfall 001	Average	52	1,715	3,780
	Range	38-64	1,270-2,082	2,800-4,590
Outfall 200	Average	3	25	55
	Range	1-5	9034	20-75

Parameter	Company Data July 1974 (mg/l)	EPA State Survey August 1974		
		(mg/l)	(kg/day)	(lb/day)
BOD_5	66-660	170	37	82
BOD_{30}	--	1,020	222	490
COD	260-1,240	410	91	200
TSS	8-110	40	9	20
TDS	1,660-2,800			
NH_3-N	188-350	295	66	145

DEVELOPMENT OF NPDES PERMIT

Average daily load limitations were prescribed for Lilly, Lafayette by 1977 based upon the average of the better performing treatment situations across the pharmaceutical industry. The Lafayette permit closely approaches the norm of waste load reductions previously written into a series of other permits on similar type pharmaceutical plants. Specifically, BOD, COD and TSS reductions based upon maximum monthly raw waste loads were respectively 94.9 percent, 79.4 percent, and approximately 80.0 percent. The 1977 average daily loads were limited to 1,540 kg (3,400 lb)/day BOD; 11,340 kg (25,000 lb)/day COD; and 1,130 kg (2,500 lb)/day TSS. Maximum daily allowable limits were approximately double the average daily limits. Ammonia nitrogen limitations for 1977 were established as 500 kg (1,100 lb)/day for the average daily condition and 1,130 kg (2,500 lb)/day as a maximum daily limit. Tippecanoe could technologically, but perhaps not economically, reduce future unoxidized nitrogen loads to considerably lower levels.

Temperature was not perceived a problem with Outfall 002 and 003, but constitutes potential concern with Outfall 001. Average temperatures for the 001 effluents are in the range of 32-36 °C (89-97°F), but individual daily temperatures have exceeded 38 °C (100°F), occasionally reaching 41 °C (105°F). The State has decided that the Wabash River demonstrates sufficient dilution to preclude any thermal impacts. Temperature limitations were not found necessary although careful monitoring will be required.

The May 1974 discharge permit application of Lilly, Tippecanoe reported relatively high average concentrations of trace metals and ions in Outfall 001: aluminum - 2.0 mg/l, chromium - 0.58 mg/l, and phenolics - 0.83 mg/l. Lead was reported as less than 1.0 mg/l and mercury was indicated of probable concern from other sampling information.

Other data shows that the same parameters are relevant for Outfall 002. The average daily limit for mercury was set at 0.045 kg (0.1 lb)/day, whereas concentration limits for chromium, phenolics, and lead were established as 0.25 mg/l, 0.25 mg/l and 0.1 mg/l, respectively. In the permit, fecal coliforms were not to exceed 200 and 400 organisms/100 ml respectively for the average daily and maximum daily conditions. The permit further specified that 96-hour TL_m fish bioassay data would be collected every 6 months for each outfall.

PHARMACEUTICAL INDUSTRY

CASE HISTORY C

PFIZER, INC., VIGO PLANT
TERRE HAUTE, INDIANA

(FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PLANT)

PFIZER, INC., VIGO PLANT, TERRE HAUTE, INDIANA
(FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PLANT)

BACKGROUND

Located in Vigo County near Terre Haute, the Vigo Plant is a bulk pharmceutical manufacturing facility producing antibiotics and synthetic organic chemicals. The Pfizer Ag Research Center is adjacent to the manufacturing plant. These facilities are spread over a land area of 810 hectares (2,000 acres) of which 65 hectares (160 acres) are used for waste treatment and up to 320 hectares (800 acres) are cropland potentially available for sludge disposal. Current employment is about 550 persons. The pharmaceutical plant operates essentially continuously.

As best determined, the Vigo Plant manufactures four different antibiotics by fermentation processes. The 1971 discharge permit application lists Streptomycin and Terramycin as two of these. The other two are considered by the Company to be confidential information. The antibiotics are manufactured to a nearly finished state with final purification and refining conducted elsewhere, presumably at Pfizer plants in Groton, Connecticut and/or Brooklyn, New York. Penicillin is also handled at the Vigo Plant but is received as the highly purified compound and packaged only.

Production rates of crude antibiotics fluctuate rather widely throughout the year. During 1972, the monthly production of the four antibiotics ranged from 0 to 71 percent of the theoretical plant manufacturing capacity (111). One antibiotic was not manufactured for ten of the months in 1972 and production reached only 8 percent of capacity in the other two months. For the other three antibiotics, monthly production ranged from none to 58, 71 and 38 percent, respectively, in comparison to full capacity.

In early 1971, corn meal and soybeans were reportedly used as raw materials for fermentation. The Company reported that during 1972 more than 72 different raw materials were employed in the production of antibiotics and synthetic organic chemicals.

Two major synthetic chemicals, fumaric acid, and benzoic acid and its derivatives, (e.g. sodium benzoate), are manufactured. Fumaric acid is used for food acidulation and is also widely used in the plastics industry. Sodium benzoate enjoys very broad use as a preservative for food products. Benzene is converted by catalytic oxidation to maleic acid which in turn is isomerized to fumaric acid. Toluene is air oxidized with the concurrent use of co-napthenate catalyst to generate benzoic acid. Untreated constituents remaining from benzoic acid processing may include benzol, diphenyl, benzophenone and anthraquinone.

Fumaric acid production was doubled in late 1970. During 1972, monthly fumaric acid production ranged from 8 to 90 percent of plant capacity (111). Manufacturing of benzoic acid and its derivatives ranged from 44 to 100 percent of capacity.

The Pfizer Ag Research Center represents peripheral but important activities. Research and development are carried out on improving food supplements for animals including dogs, cattle, hogs, chickens, and turkeys with emphasis on poultry. Up to a few hundred animals, mostly small species, are maintained at any one time at the Ag Research Center. Studies are primarily nutritional although medicinal evaluations may also be conducted. The latter may involve introduction of scours followed by efforts to cure the disease. No vaccine use is reported. Another such evaluation involves the dehorning of cattle by chemical or other means. Certain animals may be sacrificed. Animal carcasses are generally disposed of by incineration. Radiotracer studies are conducted but only infrequently. Animals subjected to radiotracers may be subsequently interred at a specially-designated burial site. Wastewaters generated by the Ag Center, thought to consist of laboratory wastes, floor and equipment washings, some pan wastes and sanitary wastes, are piped a considerable distance to the main waste treatment works.

Spent cooling waters and treated wastewaters are discharged to Jordan Creek, a very small stream originating on Pfizer property. Pfizer effluents comprise the entire dry weather flow of the creek near its source (113). Jordan Creek is a tributary of Honey Creek, another small stream that terminates in the lower Wabash River. Both Jordan and Honey Creeks are classified for agricultural water use and fish propagation.

Information used in the evaluation of the Vigo Plant was obtained from a variety of sources. Two papers by Company personnel were made available. These were a paper presented by Johnson before the Water Quality Committee of the Wabash Valley Association in November 1971 (113), and a paper by Kindrick and Johnson on wastewater treatment at the Vigo Plant presented to the EPA Effluent Standards and Water Quality Information Advisory Committee (ESWQIAC) at Purdue University in May 1973 (111). Waste source data was available from the original 1971 discharge permit application and from an April 1972 survey conducted by EPA's Evansville, Indiana, field station. Survey results included data on the quality of Jordan Creek at the plant boundary. The Vigo Plant was visited by NFIC-Denver on June 18 and 20, 1974. The Company provided follow-up information on July 10 and again on July 19, 1974. During June 1974, information on the plant in the files of the Indiana State Board of Health was compiled including monthly waste treatment performance sheets submitted to the State by the Company.

WASTE TREATMENT AND CONTROL

Water Use

The 1971 discharge permit application showed plant water supply averaging 22,000 m^3/day (5.8 mgd), derived entirely from groundwater. Water use included 17,600 m^3/day (4.65 mgd) for cooling purposes, 4,700 m^3/day (1.25 mgd) for process needs and 1,100 m^3/day (0.30 mgd) for boiler feed. About 1,500 m^3/day (0.4 mgd) of cooling water was reused for process water and boiler feed supply. Current plant water use averages 24,600 m^3/day (6.5 mgd).

Waste Sources

As shown in Table C-1, more than three-fourths of the cooling water is used in the fermentation and antibiotic recovery sectors of the plant. These same sectors, plus the organics sector, discharge most of the process wastewaters with the antibiotic recovery sector contributing a major portion.

Table C-1.
Relative Magnitude of Cooling Water Use and Process Wastewater Discharges by Operational Sector

Sector	Cooling Water Use (Percent)	Process Sewer Wastewaters (Percent)
Organics	7	16
Fermentation	47	10
Recovery of Antibiotics	35	61
Boiler and Compressor Houses	6	6
Pharmaceutical Packaging	2	3
Farm, Ag R & D	1	4
Wastewater Treatment	2	0
Total	100	100

Wastewater in the "spent cooling water" stream includes spent condenser and jacket cooling water, boiler blowdown, and barometric condensates. The condensates are believed to be about 3,780 m^3/day (1.0 mgd) or about 20 to 25 percent of the total spent cooling water stream. About 1,500 m^3/day (0.4 mgd) of once-through jacket water are reused in vacuum barometric condensers. The Company indicated that the following seven barometric condensers are present: a three-stage unit rated at 2,460 l/min (650 gpm) and operated 10 percent of the time, a single-stage unit rated at a few hundred gpm and operated 45 to 50 percent of the time, a second similar single-stage unit operated 80 percent of the time, three small units in the chemical recovery and refining sectors, and a small unit serving ion exchange operations at the water treatment facility. When the largest unit is operating, barometric condenser flows can easily exceed 3,780 m^3/day (1.0 mgd). York demisters are believed available on only one of the units. The Company considers entrainment control to be about normal for all units.

The Company reports there are no central solvent recovery facilities at the Vigo Plant. However, aqueous solvents are extensively employed in place of conventional hydrocarbon solvents within antibiotics purification processes. This should appreciably reduce the potential raw waste loads going to treatment. Foamovers from the various fermenters are directed to the industrial waste treatment plant.

The manufacturing operations produce large volumes of semi-solid and solid waste materials. The Company reports that about 11,470 m^3 (15,000 yd^3) of such wastes are generated annually. This is believed to be equivalent to about 9 kkg (10 tons) of dried waste solids that must be disposed of daily. Heel and still bottom discards total about 3,800 l (1,000 gal) weekly. These materials are all generally disposed of by landfill.

Mycelium filtered out of the fermentation broths was estimated in 1972 as amounting to around 7,650 to 15,300 m^3 (10,000 to 20,000 yd) annually. This mycelium was believed to be disposed of at the Vigo County Sanitary Landfill. For Terramycin broths, the mycelium is filtered out from the broth prior to extraction of the active ingredient. Conversely, Streptomycin is a whole broth process wherein mycelium separation is not absolutely necessary. With Streptomycin, the exhausted or spent broth together with the finely-divided mycelium all end up in the process waste treatment works. At the Vigo Plant, practically all spent fermentation broths and a significant portion of the mycelium are delivered to the waste treatment facility. The waste load to the treatment facility was substantially increased in 1972. The Company's Final Waste Treatment Plans submitted to the State in 1971 indicated that ... "A spent broth from the Streptomycin antibiotic manufacturing process in the past (had) been dried and used for feed supplement. (However) decreased demand for the by-product makes drying economically unfeasible. The Company proposes to enlarge the existing waste treatment facilities to treat the added load." The enlarged treatment facilities were completed in 1972.

Waste Treatment

History of Treatment Facilities - 1947 to 1973 -- The Vigo Plant site was originally leased from the U. S. Government in 1947. Until 1958 when the facility was purchased by the Company, waste treatment was provided by the original treatment works consisting of two clarigesters, two trickling filters, two clarifiers and chlorination facilities. The sizes of these units designed to handle an influent BOD load of 680 kg (1,500 lb)/day are shown in Table C-2. It quickly became obvious that the existing treatment was inadequate for the industrial waste loads generated. From 1949 through 1958, the "excess" wastes were handled by anaerobic lagooning, spray irrigation of high-level BOD liquors onto nearby fields and concentration and drying of waste liquors.

A substantial increase in both production and waste treatment capacity has occurred since 1958. An aeration pond and a final polishing pond [Table C-2] were completed in 1960. Mechanical surface aerators were added to the aeration pond in 1966. A large sludge stabilization pond was added in 1967. No effluent is permitted from this pond. Also, in 1967, a bio-oxidation trickling filter tower was added, operating in series with the original plant trickling filters.

Table C-2
Summary of Waste Treatment Units
Vigo Plant, Pfizer, Inc., Terre Haute, Indiana

Treatment Unit	Aerators	Volume	Dimensions	Detention Time	Remarks
Clarigesters (2)		760 m^3 (200,000 gal.)		4.1 hr	Original Plant
Trickling Filters (2)			13.7 m dia x 1.1 m deep (45 ft dia x 3.5 ft deep)		Original Plant
Clarifiers (2)		280 m^3 (75,000 gal)	12.2 m dia (40 ft dia)		Original Plant
Aeration Pond(s)	six-20 HP	28,000 m^3 (7.5 million gal)	3.0 hectare (7.5 acre) 1.2 m deep (4 ft deep)		1960 Addition Aerators added in 1966 Divided into two equal ponds in 1974
Final Polishing Pond			14 hectare (35 acre) 1.2 m deep (4 ft deep)	30 days	1960 Addition
Sludge Stabilization Pond			16 hectare (40 acre)		1967 Addition
Trickling Filter Tower		1,130 m^3 (40,000 ft^3)	12.2 m dia x 9.6 m high (40 ft dia x 31.5 ft high)		1967 Addition
Holding Pond (Cooling Water)	three-5 HP	18,900 m^3 (5 million gal)	0.3-1.2 m (1-4 ft) deep	1 day	1968 Addition
Extended Aeration Pond	five to eight-75 HP	17,400 m^3 (4.6 million gal)	85 m x 85 m x 3 m deep (280 ft x 280 ft x 10 ft deep)	6.2 days	1969 Addition
Extended Aeration Pond	five to eight-75 HP	17,400 m^3 (4.6 million gal)	85 m x 85 m x 3 m deep (280 ft x 280 ft x 10 ft deep)	6.2 days	1972 Addition
Aerobic Sludge Digester	three to five-75 HP	9,460 m^3 (2.5 million gal)	59 m x 84 m x 3-4 m deep (194 ft x 274 ft x 10-13 ft deep)		1969 Addition
Earthen Settling Basins					
Primary		260 m^3(69,000 gal)		1.1 hr	1972 Addition
Secondary		400 m^3(105,000 gal)		1.7 hr	1972 Addition
Chlorine Contact Tank		946 m^3(250,000 gal)		4 hr	

In 1968 a holding pond for retention of spent cooling waters prior to discharge to Jordan Creek was constructed. This is currently the only control provided for this waste stream.

An extended aeration pond was installed in 1969 to provide first stage biological treatment of process wastes prior to discharge to the original treatment works. An aerobic sludge digestion pond equipped with mechanical surface aerators was also installed in 1969 to handle excess sludge.

The waste treatment works handling process wastes, but exclusive of spent cooling waters, were described in 1971 as receiving 3,520 m^3/day (0.93 mgd) waste influent rated at 2,700 mg/l BOD equivalent to a raw waste load of some 9,500 kg (21,000 lb) of BOD/day (113). The treated effluent averaged 26 mg/l BOD which approximated 90 kg (200 lb) of BOD/day in the final discharges. On the basis of process wates, BOD removal through the 1971 treatment works was rated at 99.0 percent. The 3,520 m^3/day (0.93 mgd) of treated process flows were combined with 13,200 m^3/day (3.5 mgd) of spent cooling waters before discharge. Detention time in the overall waste treatment works was reported by the Company as amounting to 60 days which is noteworthy.

Disposal of excess sludge presented continuous problems at the Vigo Plant and in early 1971 it was evident the system was significantly overloaded with respect to sludge being generated. The clarifiers were not performing satisfactorily, anaerobic conditions prevailed in the 3 hectare (7.5 acre) aeration pond, and there was significant risk that anaerobic conditions and serious odors would develop around the large sludge stabilization lagoon. The sludge storage/stabilization pond plus the aerated sludge digestion pond simply had inadequate capacity for the sludge loads being experienced. Accordingly, in mid-1971, two sludge conveyance and disposal "vehicles" were pressed into service together with a heavy-duty farm tractor. Excess sludge was drawn directly from the clarigesters at the treatment works. The sludge was injected into a narrow furrow 15 to 38 cm (6 to 15 in.) below the ground surface in a procedure quite similar to anhydrous ammonia injection. From June to November 1971, over 13,200 m^3 (3.5 million gal.) of sludge was injected into Pfizer-owned farmlands. Some 160 hectares (400 acres) were used for sludge disposal through 1973. The subsurface sludge injection program was reported carefully controlled. In order to protect crops, the application rates of organic and inorganic nitrogen combined were limited to a maximum of 140 kg (300 lb)/ acre annually.

In September 1971, the State gave approval for further expansion of the waste treatment works at Vigo. Additional units consisted of a second extended aeration pond (presumably similar to the pond installed in 1969) equipped with floating mechanical aerators and two auxiliary earthen settling basins [Table C-2]. These relatively small basins consist of a primary settling and grit removal cell and a secondary settling cell through which activated sludge is recycled from the effluent side back to the influent side of either of the extended aeration ponds. The two extended aeration ponds are arranged so that they may be operated either in parallel or in series. The expanded treatment plant was completed in 1972 with the capacity to handle 5,700 to 7,600 m^3/day (1.5 to 2.0 mgd) of process flows containing a raw waste load around 13,600 kg (30,000 lb) of BOD/day (113).

Current Waste Treatment Practices--The current (mid-1974) waste treatment system for the Vigo Plant consists essentially of all the treatment units constructed through 1972 listed in Table C-2 with minor modifications. The units are connected in a manner to provide five-stage biological treatment of process wastewaters. The stages in order of downstream progression are an extended aeration activated sludge plant, a two-stage trickling filter plant composed of the original (pre-1947) waste treatment works and the bio-oxidation high-rate trickling filter, an aerated stabilization pond, and a final polishing pond. Spent cooling water passes through a separate holding pond, the only control measure.

The extended aeration stage consists of the extended aeration pond constructed in 1969 and the second pond and two earthen settling basins completed in 1972 [Table C-2]. Process wastes initially enter the earthen primary clarifier. Settled sludge goes either to land disposal or the aerobic digester.

Primary clarifier effluents enter the extended aeration activated sludge basins which may be operated either in a parallel or series arrangement. During the field inspection of June 20, the basins were operating in series as is generally the case. The MLSS in the extended aeration basins were reported usually between 2,000 and 4,500 mg/l. Effluent from the extended aeration basins receives settling in an earthen secondary clarifier with an overflow rate of about 20.4 m^3/m^2 (500 gal./ft^2)/day. Secondary sludge is returned to the aeration basins or taken to land disposal.

The effluent from the extended aeration stage passes to the two clarigesters operated in parallel. The overflow rate is about 19.4 m^3/m^2 (475 gal./ft^2)/day. Settled sludge at about 1.5 percent solids content is sent to land disposal, the aerobic digester, or possibly back to the extended aeration basins.

Clarigester effluents are applied onto two standard-rate trickling filters operating in parallel. Hydraulic loading is around 49 m^3/m^2 (1,200 gal./ft^2)/day and the organic loading is about 10.7 kg/m^3 (670 lb BOD/1,000 ft^3). Effluents are applied next in series to a high-rate, plastic-media, bio-oxidation tower. Wastewaters leaving the trickling filter units enter into a final clarifier. Sludge is unloaded to the clarigesters, to the aerobic digester, or to the sludge stabilization pond.

Final clarifier flows were previously sent to the 3.0 hectare (7.5 acre) aerated stabilization pond. However in early 1974 this particular pond was divided into two equal aerated ponds operating in series. In June 1974, all six aerators were situated in the first pond and the Company was planning to install additional aerators in the second pond as soon as possible.

Overflow from the two aerated ponds next passes to the large final stabilization or polishing pond. There is no supplementary aeration in this pond which has a detention time of 30 days or slightly greater. Effluent from the final stabilization pond is passed through a chlorine contact box with a rather large capacity of 946 m^3 (250,000 gal.) providing about 4 hr detention. Due to the nature of the wastewater and/or the long detention in the box, no chlorine residual is observed in the final effluent. This effluent (Outfall 001) intercepts Jordan Creek immediately below the spillway overflow of the spent cooling water retention pond.

The aerobic sludge digestion unit is a pond with a sludge holding capacity of 9,460 m^3 (2.5 million gal.) and is equipped with mechanical floating aerators for relatively heavy aeration. Sludge at 3-5 percent solids is removed from this unit for disposal into the sludge stabilization pond. Sludge removal rates are 300 m^3/day (80,000 gpd) if the solids content is 3 percent but less at higher solids content. Sludge holding and disposal facilities are much more critical over the colder winter periods.

The sludge stabilization pond receives a relatively low loading of mostly stabilized sludges and no overflow is reported. Evaporation is slightly in excess of rainfall. Sludge banks are slightly exposed at the center of the pond and the remainder of the sludge deposits are submerged under the overlying waters or supernatants. No odors are reported whatsoever from this operation by the Company and none were observed during the plant visit.

As indicated previously, disposal of excess sludge by sub-surface injection into cropland was begun in 1971. In addition to this practice, sludge is now being applied to growing crops in side-dressing fashion. Up to 320 hectares (800 acres) of Company-owned cropland are available for this purpose with about half in actual use through 1973. It is reported that every effort is made to minimize runoff from the fields receiving sludge dosing. Pfizer is applying sludge to the soil in the wintertime except for about 60 days when the weather is most severe. Crops include winter wheat, corn and soybeans. The fields are apparently leased to local farmers who harvest the crops. About 64 mm (0.25 in.) of sludge is deposited during each application which is equivalent to 38 m^3 (10,000 gal.)/acre/application. Since the water table is about 46 to 55 m (150 to 180 ft) below ground surface, the Company feels there is little or no hazard to ground water. Quality of groundwaters in the sludge application sectors is being monitored, especially for nitrate and phosphate levels (113). Unfortunately, little or no data is apparently collected by the Company on survival of pathogenic microorganisms possibly associated with sludge injection practices. Adequate data would be welcome on this subject. Pfizer reports no prevailing odors associated with these sludge disposal practices.

The cooling water impoundment pond provides about one-day detention for spent cooling waters and possibly some surface runoff emanating from the Vigo Plant. No treatment is provided for the mixed cooling waters before release to the pond. The pond is equipped with floating mechanical aerators. This pond was heavily laden with algae during the plant visit in mid-June 1974. The Pfizer waste treatment system is somewhat unusual in that overall process wastewater detention time in the system, discounting cooling waters, is in the range of 45 to 60 days. In the power cost area, the various aerators in the system add up to a total of 1,100 to 1,200 HP. Together with the other electrical-consuming equipment in the network, Pfizer personnel in June 1974 estimated a total waste treatment power need of perhaps 1,400 to 1,500 HP. These figures are not completely verified and may be on the high side. Pfizer could not conveniently break out power costs attributable solely to treatment but did indicate that 1,500 HP would be equivalent to around $8,000 per month or $80,000 to $90,000 annually for electrical power costs.

WASTE LOADS

NPDES Permit Application

The original NPDES permit application submitted in 1971 summarized average conditions for 1970-71 and the combined cooling water and treated process waste effluents [Table C-3].

Table C-3.
Permit Application Data

Parameter	Concentration (mg/l)	Lead	
		(kg/day)	(lb/day)
BOD	14	280	610
COD	80	1,600	3,500
TOC	18	360	790
Total Solids	932	18,500	40,800
TSS	40	770	1,700
Ammonia-N	33	680	1,450
Organic-N	24	490	1,070
Kjeldahl-N	56	1,100	2,450
Sodium	164	3,270	7,200
Phosphates as P	19	380	830
Sulphates	146	2,900	6,400
Iron	2	40	88
Oil and Grease	0	-	-
Coliforms	Reasonably high levels		
Trace Metals	Little data given		
Phenolics	0		-
Flow	a/		

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a/ Flow given as 19,900 m^3/day (5.25 mgd) for the combined effluent including 4,900 to 5,200 m^3/day (1.3 to 1.5 mgd) of process wastewaters.

1972 EPA Survey Results

A survey of wastewater effluents and receiving waters in and around the Vigo Plant property was conducted in April 1972 by EPA's Evansville, Indiana, field station. Summary results are given in Table C-4 for the treated process wastewater effluent and for Jordan Creek downstream of both the process wastewater and spent cooling water discharges. Flow rates for the process and cooling water effluents during the survey were estimated at 4,200 and 15,500 m^3/day (1.1 and 4.1 mgd), respectively.

Table C-4
Summary of 1972 EPA Survey Results

Parameter	Treated Process Effluent (mg/l)	Jordan Creek at Northerly Plant Property Line(mg/l)
BOD	30 to 40	10 to 12
COD	440	80
TOC	145	33
Ammonia-N[a]	145	20
Kjeldahl-N[a]	185	28
Phosphorus, total[b]	45	6.8
Arsenic	0.01	-
Cadmium	0.002	-
Chromium, total	0.03	-
Copper	0.03	-
Fluoride	0.20	0.22
Iron	2.60	-
Lead	0.02	-
Manganese	0.25	-
Mercury	0.0017	-
Nickel	0.10	-
Zinc	0.06	-
Fecal Coliforms/100ml.	690	20
Color (units)	60	-

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[a] Ammonia and Kjeldahl-N content of raw process waste respectively analyzed as 125 and 280 mg/l.

[b] Phosphorous content of raw process waste analyzed as 88 mg/l.

The April 1972 survey showed the raw process wastes at that time as having 125 mg/l ammonia-N and 280 mg/l Kjeldahl-N (i.e. Kjeldahl-N equals ammonia plus organic nitrogen). The process stream after passing through the treatment works contained 145 mg/l ammonia-N (a 12 percent increase), whereas the final Kjeldahl-N content was 185 mg/l (a 34 percent decrease). With many pharmaceutical plant effluents, excessive amounts of ammonia and organic nitrogen are present even after extensive biological treatment, and this is likewise the case for the Vigo Plant. Nitrogeneous wastes originate both from the fermentation and the synthetic organic chemical manufacturing sectors.

During the EPA survey, analytical problems were encountered with respect to the BOD test because of the nature of the wastes. Consequently, estimates only were given for BOD values if no analytical control problems had occurred, and furthermore, only possible ranges in BOD values were reported. The EPA survey showed high values for iron, phosphorus, and ammonia and organic nitrogen.

Company Data

Pfizer collects extensive data on its process wastewater stream both before and after treatment. In contrast, only limited data is available on the spent cooling water stream.

A 1973 Pfizer status report presented extensive treatment data for the 1972 operational year and additional data for 1973(111). Process wastewater flows averaged 4,430 m^3/day (1.17 mgd) during 1972. Average 1972 treatment results are shown in Table C-5.

Table C-5
Summary of 1972 Process Wastewater Treatment Results

Parameter	Influent (mg/l)	Influent (kg/day)	Influent (lb/day)	Effluent (mg/l)	Effluent (kg/day)	Effluent (lb/day)	Percent Removal
BOD	1,480	6,670	14,700	27	120	264	98.0
TSS	1,020	4,540	10,000	25	111	244	97.5

On a monthly average basis, raw process waste loads discharged to the treatment facility varied from 910 to 9,070 kg (2,000 to 20,000 lb) of BOD/day and from 450 to 6,800 kg(1,000 to 15,000 lb) of TSS/day. A very substantial majority of the BOD was removed in the extended aeration basins and the trickling filter units, leaving relatively little BOD going through the final polishing ponds. On the other hand, low TSS levels were not attained until passing through the final 3 and 14 hectare (7.5 and 35-acre) stabilization ponds.

Data reported for 1972-1973 on the combined treated process and spent cooling streams are summarized in Table C-6 (111). The data on iron, phosphorus and ammonia nitrogen will be discussed in more detail in a following section.

Table C-6
Residual Pollution Loads, Combined Process Plus Cooling Water Discharges
1972-1973

Parameter	Concentration (mg/l)	Load	
		(kg/day)	(lb/day)
Flow			
Low		15,670[a/]	4.4[b/]
Normal		19,870[a/]	5.25[b/]
High		29,530[a/]	7.80[b/]
BOD	10	200	440
TSS	22	438	965
Iron	2	40	88
Phosphorus as P	19	380	830
Ammonia N	40	770	1,700

[a/] Flow in m^3/day
[b/] Flow in mgd

Pfizer generally analyzes treatment plant inflow and effluent on a daily basis for BOD and solids; COD results are lacking throughout the system. An extended series of results on BOD and TSS concentrations and loadings for the period January 1973 to May 1974 and covering the process waste stream both before and after treatment, the cooling water stream, and Jordan Creek at the Company downstream property line, is summarized in Tables C-7 and C-8.

The process waste system is providing better than 99 percent removal of BOD according to recent monthly performance reports by the Company and also 1973-74 data [Table C-7]. Biochemical oxygen demand removal over the period of 17 months through May 1974 averaged 99.1 percent with a residual of 73 kg (160 lb)/day BOD in the treated effluent. Corresponding average TSS removals for the process waste stream have been 97.8 percent yielding a residual load of 132 kg (290 lb)/day TSS in the treated effluent [Table C-8]. The treated process stream has been generally running 10 to 20 mg/l BOD, and 20 and 40 mg/l total suspended solids. The ratio of COD to BOD in the Pfizer treated effluent appears to be in the range of 5.5 to 6.0, and COD values for the treated process stream approximate 60 to 80 mg/l.

Table C-7
Summary of Monthly BOD Data for Waste Treatment Facilities, Cooling Water and Jordan Creek
January 1973 through May 1974

Month	Treated Flow		Process Raw Waste			Treated Effluent			Removal	Cooling Water[a/]			Combined Effluents[a/]		Jordan Creek @ Property Line
	(m^3/day)	(mgd)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	(Percent)	(mg/l)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(mg/l)
Jan. 1973	5,750	1.52	1,100	6,270	13,820	10	54	120	99.1	5	83	190	141	310	5
Feb.	5,600	1.48	1,470	8,300	18,300	10	54	120	99.3	7	118	260	172	380	7
March	5,980	1.58	1,250	7,300	16,100	10	64	140	99.1	9	154	340	218	480	8
April	5,830	1.54	1,340	7,440	16,400	15	82	180	98.8	5	86	190	168	370	9
May	4,580	1.21	2,190	8,070	17,800	19	91	200	98.9	6	104	230	191	420	-
June	5,380	1.41	2,050	10,160	22,400	29	159	350	98.4	6	104	230	263	580	18
July	4,730	1.25	1,640	7,440	16,400	19	95	210	99.0	5	86	190	181	400	14
Aug.	2,910	0.77	900	2,400	5,300	17	41	90	97.9	5	86	190	127	280	12
Sept.	4,160	1.10	2,200	9,530	21,000	12	54	120	99.5	5	86	190	141	310	8
Oct.	4,130	1.09	2,340	9,890	21,800	20	77	170	99.1	5	86	190	163	360	11
Nov.	4,160	1.10	2,100	9,160	20,200	12	45	100	99.5	6	104	230	150	330	10
Dec.	4,850	1.28	1,700	9,390	20,700	9	50	110	99.5	6	104	230	154	340	8
Jan. 1974	5,410	1.43	1,570	8,800	19,400	12	68	150	99.3	6	104	230	168	370	8
Feb.	4,850	1.28	2,190	8,850	19,500	13	64	140	99.3	7	118	260	181	400	9
March	5,070	1.34	1,820	8,710	19,200	11	59	130	99.4	6	104	230	159	350	10
April	5,070	1.34	1,770	7,030	15,500	16	82	180	98.8	6	104	230	181	400	11
May	5,490	1.45	1,950		-	17	104	230	-	6	104	230	209	460	9
Average, 1973-74	4,920	1.30	1,740	8,050	17,740	15	73	160	99.1	6	102	225	175	385	10
$\bar{x} + 2\sigma$[b/]							106	233					204-227	450-500	

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a/ Average spent cooling water flows assumed to be 17,000 m^3/day (4.5 mgd). Combined treated process plus cooling water flows therefore equal to an average of 21,960 m^3/day (5.8 mgd).

b/ Excludes June 1973.

Table C-8

Summary of Monthly TSS Data for

Waste Treatment Facilities, Cooling Water and Jordan Creek

January 1973 through May 1974

Month	Treated Flow		Process Raw Waste			Treated Effluent			Removal	Cooling Water[a/]			Combined Effluents[a/]		Jordan Creek @ Property Line
	(m^3/day)	(mgd)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	(Percent)	(mg/l)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(mg/l)
Jan.1973	5,750	1.52	760	4,373	9,640	17	91	200	97.9	15	254	560	345	760	13
Feb.	5,600	1.48	1,080	6,051	13,340	22	127	280	97.9	10	172	380	299	660	14
March	5,980	1.58	870	5,203	11,470	22	118	260	97.7	14	240	530	358	790	35
April	5,830	1.54	900	5,248	11,570	30	163	360	96.9	12	204	450	367	810	21
May	4,580	1.21	2,760	12,642	27,870	23	95	210	99.2	4	68	150	163	360	--
June	5,380	1.41	1,360	7,258	16,000	43	250	550	96.6	4	68	150	318	700	37
July	4,730	1.25	1,450	6,863	15,130	35	181	400	97.4	6	104	230	281	620	21
Aug.	2,910	0.77	210	612	1,350	26	68	150	88.9	23	390	860	463	1,020	32
Sept.	4,160	1.10	1,920	7,992	17,620	24	100	220	98.8	5	86	190	186	410	9
Oct.	4,130	1.09	2,460	10,152	22,380	40	159	350	98.4	9	154	340	313	690	16
Nov.	4,160	1.10	1,520	6,328	13,950	24	95	210	98.5	9	154	340	250	550	16
Dec.	4,850	1.28	1,150	5,570	12,280	27	91	200	98.4	15	254	560	345	760	32
Jan.1974	5,410	1.43	1,720	9,312	20,530	28	141	310	98.5	8	136	300	277	610	18
Feb.	4,850	1.28	1,150	5,570	12,280	21	100	220	98.2	19	322	710	422	930	21
March	5,070	1.34	1,230	6,237	13,750	23	123	270	98.0	13	222	490	345	760	24
April	5,070	1.34	1,240	6,291	13,870	46	222	490	96.5	33	563	1,240	785	1,730	46
May	5,490	1.45	1,420	7,802	17,200	27	145	320	98.1	18	309	680	454	1,000	21
Average, 1973-74	4,920	1.30	1,365	6,668	14,700	28	132	290	97.8	13	218	480	349	770	24
$\bar{x} + 2\sigma$ [c/]							207	457							

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a/ Synthesized from monthly TSS concentrations previously provided by Company.

b/ Average spent cooling water flows assumed of, 17,000 m^3/day (4.5 mgd). Combined treated process plus cooling water flows therefore equal to an average of 21,960 m^3/day (5.8 mgd).

c/ Excludes June 1973.

The cooling water stream receiving no treatment contributes a like organic and solids loading but in a much larger flow. The cooling water discharge averages 5 to 7 mg/l BOD and generally 4 to 20 mg/l TSS. Over the period of January 1973 through May 1974, the average BOD and TSS loadings for the cooling water stream were observed to be 102 kg (225 lb)/day and 218 kg (480 lb)/day, respectively. Waste removals through the process waste treatment system have been exceptionally high. But if the BOD and TSS loads contained in the cooling water stream are added overall removals in the Pfizer system are then slightly reduced to about 98 percent for BOD and 95 percent for total suspended solids.

The plant has a potential iron problem in its wastewater effluents even though some of the local surface receiving streams are fairly high in iron content. Pfizer combined treated process and cooling water flows contain around 2.0 mg/l Fe; in June 1974 the total discharge was running about 1.7 mg/l Fe. Company data shows the cooling water flows contain around 1.2 mg/l Fe, and the treated process flows around 2.6 mg/l for a discharge total load of 32 to 41 kg (70 to 90 lb) Fe/day. Importantly, Company results illustrate only 0.2 mg/l Fe in the intake ground waters as compared to 6.0 mg/l in the raw process wastewaters. According to Pfizer, the incremental iron contributed to final discharges mostly arises from tank corrosion although some is believed to originate from raw materials used in fermentation. No iron salts are purchased by the Company. There is no data available on corresponding manganese levels in effluents. In June 1974 the effluent from the treatment plant was observed to have a relatively persistent yellow color. The Vigo Plant by virtue of improved in-plant practices is believed easily capable of reducing iron levels in the future down to 1 mg/l, equivalent to a total discharge load of around 23 kg (50 lb)/day.

In June and July 1974, Pfizer, Inc., provided the EPA with significant data on nitrogenous loads in the waste treatment system and removal efficiencies of ammonia, organic and Kjeldahl nitrogen through the system. During the plant visit of June 1974, the Company indicated that ammonia-N in the treatment works varies from a low of 15 mg/l in the summertime to a high of 130 mg/l or greater during the winter months. The Company also stated that just recently a concentrated ammonia waste stream amounting to 140 to 180 kg (300 to 400 lb) ammonia daily had been removed from the Pfizer circuit and was now being sold for its by-product nutrient value to a nearby industrial plant. Long-term ammonia data collected by the Company during both summer and wintertime periods showed the following values: raw process wastes - 75 to 235 mg/l; treated process stream - 5 to 75 mg/l; spent cooling water stream - 0 to 6 mg/l; and Jordan Creek near Pfizer northerly property line - still relatively high at 5 to 40 mg/l. In June 1974, Pfizer personnel indicated they believed that direct ammonia toxicity to fishlife could indeed become evident in the ammonia range of 2.5 to 25 mg/l.

Pfizer iniated intensive nitrogen data collection over the period of May 29 through June 2, 1974, and this information shows the treatment system is capable, at least during late spring and early summer, of removing considerable Kjeldahl, ammonia and organic nitrogen waste loads [Table C-9]. Again it is noted that wintertime nitrogenous levels are generally higher than summertime results in this situation. Ammonia and organic nitrogen in the final discharges will undoubtedly continue to represent vexing problems for the Vigo Plant.

Table C-9.
Summary of Nitrogen Data, May 29 - June 2, 1974

Parameter	Process Wastes			Spent Cooling Water and Treated Process Wastes (mg/l)
	Untreated (mg/l)	Treated (mg/l)	Percent Removal	
Kjeldahl-N	360	87	75	21
Ammonia-N	165	53	67	11
Organic-N	194	35	81	10
Nitrate-N	1.3	10.7	-	5

DEVELOPMENT OF NPDES PERMIT CONDITIONS

Large amounts of unoxidized nitrogen in pharmaceutical plant wastes create a significant number of problems which have been elaborated upon elsewhere in this report. Many of these problems are quite serious. Best practicable technology for removal of nitrogen loads in the Pfizer process waste stream has been established as capable of yielding 20 mg/l ammonia-N, which equates to 95 kg (210 lb)/day ammonia. This load has been established in the draft NPDES permit as the average daily limit to be attained by Pfizer in 1976-7. The 20 mg/l ammonia limit is less stringent than the ammonia nitrogen levels which may be expected in the effluents from a municipal plant having reasonably good "secondary treatment" methods available. Pfizer reports they are capable in the summertime of achieving 15-20 mg/l ammonia levels, but wintertime values are much higher. In-plant modifications, recovery and/or removal, or the treatment of high-strength ammonia wastes are determined as feasible at Pfizer.

Company personnel in June 1974 indicated their treatment works is capable of removing about 50 percent of the incoming phosphorous raw waste loads. No limits have been set on the draft NPDES permit regarding phosphorous since significant phosphorous reductions are anticipated commensurate with future nitrogen removals.

Fecal coliform data by the Company covering the period January 1973 through July 1974 show a maximum value of 490 organisms/100 ml. Because of the nature of wastes involved, the draft NPDES permit has incorporated monitoring provisions and a limit of 200 organisms/100 ml for fecal coliform bacteria.

Pfizer has provided EPA with appreciable bio-assay data but for various reasons this information has not been incorporated herein. Many of the pharmaceutical permits, including that for Pfizer's Vigo Plant specify that bioassay and fish survival monitoring requirements are necessary because inherent toxicity may be found associated with pharmaceutical wastes.

PHARMACEUTICAL INDUSTRY

CASE HISTORY D

COMMERCIAL SOLVENTS CORPORATION
TERRE HAUTE, INDIANA

(FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PRODUCTION)

COMMERCIAL SOLVENTS CORPORATION, TERRE HAUTE, INDIANA (FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PRODUCTION)

BACKGROUND

The Commercial Solvents Corporation (CSC) plant at Terre Haute, Indiana, is a bulk pharmaceutical chemical and organic chemical manufacturing installation that produces a wide variety of agricultural, industrial, animal health and human health (final) products. Fermentation and a great diversity of organic chemical synthesis operations are conducted. Major products as of 1974 include monosodium glutamate, the methylamines and various methylamine derivatives, alcohols, chemical intermediates, choline chloride (an important animal feed supplement), surface active agents, waxes, enzymes, starting materials for bacteriostat and pesticide-type compounds, and a spectrum of "Baciferm" and "Bacitracin" products. Some fermentation is conducted for Eli Lilly and Company. The plant was once a major manufacturer of riboflavin (Vitamin B_2) but, due to economic reasons, these particular operations were discontinued about 6-7 years ago. Due to shortages of hydrocarbon feedstocks, the CSC plant seemed to be operating below rated capacity in mid-1974 in many manufacturing sectors, especially the methylamine synthesis and derived products.

Products associated with the CSC, Terre Haute facility are as follows:

monomethylamine
dimethylamine
trimethylamine
butyl lactate
dibutyl phthalate
tributyl phosphate
butanol
ethyl alcohol
isopropyl alcohol
"Cycloserine"
"NMPD" (intermediate)
"AMPD" (intermediate)
"NMP" (intermediate)
"NEPD" (intermediate)
"Alkaterge-C" (surface active agent)
"Alkaterge-T" (surface active agent)
Various nitroparaffinic compounds
monosodium glutamate
"Ralgro(P-1492)" (animal growth factor)
"Baciferm Soluble 50" (animal medicinal)
"Baciferm" (antibiotic/feed supplement)
choline chloride (animal feed supplement)
"Bacitracin" USP (antibiotic)
"Zinc Bacitracin" USP (antibiotic)
"Bacitracin X-1 Concentrate"
"Regular Bacitracin"
"Tris Amino" (wide variety of pharmaceutical uses)
"Bioban(P-1487)" (bacteriostat, pesticide)
Hydroxyethyltrimethyl ammonium bicarbonate (intermediate, alkaline catalyst)
Oxazoline waxes (various forms)
"Adamad Catalyst 20" (acid catalyst)
Various enzymes
"Tylosin" antibiotics (for Eli Lilly & Co.)

The plant is an old installation dating back to around the 1880's. However, extensive refurbishing and modernization have taken place in recent years. The Terre Haute plant operates continuously 24 hours per day, 7 days a week with around 600 employees.

WASTE SOURCES

The CSC plant currently has three main waste discharges to the Wabash River. These are Outfalls 001, 002 and 003 (numbered progressively in a northerly or upstream direction) located on the east (main manufacturing plant) side of the River. Three pipelines under the River convey additional wastes from the plant to an anaerobic lagoon system and a spray irrigation system on the west side. Until recently, the lagoon system effluent was discharged to the River through Outfall 004 on the west side of the River. In about January 1974, however, wastes formerly going to the lagoon system were diverted to the City of Terre Haute municipal sewerage system eliminating discharge 004. There is no surface discharge to the River from the spray irrigation system.

The philosophy of the Company has been to collect the majority of strong wastewaters for appropriate treatment and disposal. Remaining contaminated process streams have been merged with large amounts of cooling waters and discharged through Outfalls 001, 002 and 003, presumably because of the large expense that would be otherwise involved in segregating and transporting these wastes to available treatment. There is little treatment on these three lines and the volume ratio of cooling water to process wastes is roughly estimated to be in the order of 8 to 1. It is believed that the plant has reasonably high capability in shifting waste sources from one collection system to another. Given below is a comprehensive tabulation of waste sources currently contributing to Outfalls 001, 002 and 003, the waste stream previously known as Outfall 004 but now going to the city, and the concentrated waste stream directed to the spray irrigation fields.

Wastewaters Discharged to Outfall 001

-- Bottom ash sluice streams when coal is burned in the power house boilers. The boilers may be fired by gas, oil or coal fuel supply. The degree of coal burning will depend upon the relative abundance of each type of fuel.

-- Regenerants and backwashes from the hot lime-zeolite water softening operations.

-- Floor washings from the steam power plant, and from the choline chloride feed supplement preparation building; also boiler blowdowns from the steam power plant.

-- Regenerants from the MSG ion exchange columns and some possible loss of bonechar from the MSG char column(s).

-- Miscellaneous streams including undesignated tank washings, air compressor coolant flows, cooling waters from the microbiological sector, and land surface runoff.

Wastewaters are retained for a short time period within a 0.4 to 0.6 hectare (1.0 to 1.5-acre) shallow settling pond built into and alongside a coal storage pile. The pond overflow is Outfall 001. Average wastewater flow was reported as 4,160 m^3/day (1.1 mgd) by the Company in their 1971 discharge permit application, and 2,740 m^3/day (0.725 mgd) during a July 1973 EPA sampling survey of CSC outfalls.

Wastewaters Discharged to Outfall 002

- -- Overflows from the fermentation pots capturing foamovers from the CSC fermenters.
- -- Air vent discharges from fermenters which are directly exhausted into the plant sewer leading to Outfall 002.
- -- Floor washings from the warehouse area, from MSG manufacturing, and from other undefined process sectors.
- -- Barometric condenser waters from MSG manufacturing and the fermentation product sectors.
- -- Spent cooling waters from operable fermenters and spent compressor coolant flows.
- -- Unspecified wastes from Baciferm production.
- -- Roof drainage and land surface runoff.

Average wastewater flow for Outfall 002 was reported as 9,080 m^3/day (2.4 mgd) in the Company's 1971 waste discharge permit application. The flows were 10,790 to 11,020 m^3/day (2.85 to 2.91 mgd) during the July 1973 EPA field sampling study.

Wastewaters Discharged to Outfall 003

- -- Spent condensates from some 12 barometric condenser units.
- -- Floor washings from the following: chemical pilot plant, "Cat 20" production area, and the choline chloride, choline bicarbonate, butyl lactate and "Bioban" manufacturing sectors.
- -- Air scrubbing effluents from Baciferm recovery operations, and from the methylamines and choline chloride production sectors.
- -- Miscellaneous wastes including production laboratory wastes, spent cooling waters and surface runoff accruing from undesignated areas, together with drainage and runoff associated with tank farm sectors.

Discharge rate for Outfall 003 was given as 12,500 m^3/day (3.30 mgd) in the 1971 discharge permit application compared to measured values of 12,600 to 13,200 m^3/day (3.33 to 3.48 mgd) during the July 1973 EPA field survey.

Wastewaters Previously Going to Outfall 004 but Now Directed to the City of Terre Haute

- -- Air vent discharges from fermenters directly exhausted to the plant sewer.

- Vessel washings and overflows from fermentation pots within the fermentation sectors.
- Washings and discards from fermentation cookers.
- Floor washings from Baciferm recovery, zinc bacitracin and enzymes production.
- Process waste streams from the microbiological R & D plant and laboratory, the chemical pilot plant, the production laboratory and the methylamines production sector.
- Sanitary and miscellaneous spent waters.

Average wastewater flows for Outfall 004 were reported as 450 m^3/day (0.12 mgd) in the 1971 discharge permit application. This raw waste stream "now" going to city sewers was rated in July 1974 as around 570 m^3/day (0.15 mgd) containing some 2,300 kg (5,000 lb) BOD daily.

Wastewaters Discharged to the Spray Irrigation System

- Spent fermentation broths from MSG manufacturing plus other leftover fermentation broths.
- Series of process waste streams from Baciferm recovery, and the production areas for bacitracin, "Biobane," and methylamines derivatives.
- The water layer from butanol recovery.
- Various mother liquors and distillates from overall manufacturing areas.
- Floor washings from nitroparaffin and butanol derivatives manufacturing sectors.
- Washings and spent solutions from railroad tank car cleaning.

In early 1971, Company plans called for diverting solvent recovery still heels to the CSC waste treatment system. However, in June 1974 the Company indicated it had no distillation still specifically employed for waste recovery. However, a large butanol recovery still, when not used for butanol, is reported as available for refining waste solvents. It is noted that these still bottoms apparently have not yet been tied into the treatment works.

Continuing efforts are made to curb air pollution problems at the CSC, Terre Haute installation. These problems have not been completely solved to date although appreciable air scrubbing is available. Previously, air contaminants were cited as potentially originating from the Baciferm-Riboflavin rotary drive driers, the MSG processing areas, the cycloserine process, and the trimethylamines products area. As mentioned above, riboflavin is no longer manufactured at this plant.

WASTE TREATMENT AND CONTROL

History and Background

Past waste abatement objectives of the Company have been to segregate most of the high-strength waste streams from dilute wastes and to transport these concentrated materials into available waste treatment facilities located across the Wabash River from the main plant site. The strongest wastes are treated and disposed of via spray irrigation over 142 to 150 hectare (350 to 370 acres) of Company lands. An 0.8 hectare (2 acre) anaerobic pond followed by a 5.7 hectare (14 acre) aerobic stabilization pond have been employed for handling other strong wastes. The spray irrigation complex was designed for complete containment of applied wastes with no runoff to receiving streams. About 81 hectares (200 acres) of land are in current use whereas 57 hectares (150 acres) are inactive. The Company could conceivably purchase more lands for spray irrigation if necessary.

Spray disposal of strong wastewaters has been decidedly advantageous to CSC but difficulties have involved odors, excessive ponding, lack of success in maintaining suitable cover crop, potential backflooding of the irrigation site by the Wabash River, and probable salinity pickup by the irrigated soils. The anaerobic-aerobic pond system described above was designed for 95 percent BOD reduction and 98 percent TSS reduction. However, due either to the inability to reach these performance levels, excessive odor conditions, or a combination of both factors, use of the pond system has been discontinued. The Company about 8-9 months ago diverted the waste stream entering the pond system to the City of Terre Haute municipal waste treatment facilities. The lagoons are now used only for storing bad batches and spills. There were no direct discharges from the two-lagoon system to the River during all of 1973 and the first half of 1974, except for some unplanned releases that occurred in October 1973.

Three separate published reports describe the past history and waste handling practices at the plant from the early 1960's through about 1970. The first of these reports discusses test results obtained from a pilot-scale anaerobic lagoon receiving chemical and fermentation process wastes. The test criteria developed from the pilot-scale operations eventually led to design of a full-scale (20 acre) lagoon (51). In 1968, CSC issued a report upon results obtained through the spray irrigation land disposal system. Performance data on the land disposal system covered the period August 1965 until about March 1968 (11). The Company concluded that land application of pharmaceutical wastes, in this case mostly derived from fermentation processes, is a viable means of treating these low volume, high BOD spent streams. In the last published paper of 1971, CSC again focused upon the anaerobic lagoon method of treating strong pharmaceutical wastewaters. Results are given for the period covering July 1965 through March 1971 (91).

Anaerobic Lagooning, Pilot Plant Studies in the 1960's

In the early 1960's, waste treatment was apparently being considered for the first time at Terre Haute. Total effluents at that time approximated 32,600 m^3/day (8.6 mgd), but it was found that the very strong process wastes could be feasibly segregated from the relatively clean cooling and associated waters. The strongly contaminated waste streams potentially available for treatment amounted to 566 m^3/day (150,000 gpd) with a composite waste strength of about 10,000 mg/l BOD and in excess of 30,000 mg/l TSS. The BOD loading was in the area of 4,080 kg (9,000 lb)/day and the total suspended solids were roughly around 12,700 kg(28,000 lb)/day. Process waste streams varied in pH from 3.5 to 10.5. Waste loads which could not be easily segregated nor collected amounted to about 390 kg (650 lb) BOD/day and these were allowed to discharge to the River. Sanitary wastes were delivered to the city sewer system "whenever possible" (51).

The Company systematically evaluated a number of waste treatment methods including activated sludge, trickling filtration, anaerobic digestion, spray irrigation, lagooning and wet oxidation. Biological treatment by activated sludge or trickling filtration would provide high BOD removals, but pretreatment of the waste streams was thought necessary due to excess amounts of toxic metal ions present. The very strong nature of the wastes might also have caused unacceptably high unit loadings upon these treatment processes. Anaerobic digestion appeared attractive except for the somewhat long retention time required. Spray irrigation was discounted because of the prevalence of sanitary sewage and the extreme levels of nitrogen and toxic metal ions. Waste lagooning was given full consideration because of simplicity, easy solids separation, and other advantages. An aerobic lagoon was determined as requiring too much land. "Satisfactory" operation of an anaerobic lagoon was indicated probable at a unit BOD loading of around 500 kg/hectare (450 lb/ acre)/day, which in the case of CSC equated to approximately 8 hectares (20 acres) of land. Wet oxidation of the waste streams at elevated temperatures appeared meritorious, but system complexity and high initial costs represented serious constraints. The Company decided to pursue pilot-plant studies on anaerobic lagooning. Treatment objectives were to reduce total waste loads to the Wabash River down to 1,900 kg (4,200 lb) BOD/day. CSC was contemplating future raw waste loads up to 8,200 kg (18,000 lb) BOD/day. Accordingly, treatment system BOD removal efficiencies of 60-80 percent were sought in the feasibility studies.

A pilot lagoon 1.2 m x 1.2 m x 1.2 m (4 ft x 4 ft x 4 ft) was constructed for experimental treatment of strong wastes. The BOD of the feed was adjusted to about 10,000 mg/l and unspecified pretreatment was employed to convert toxic heavy metal ions to their less harmful form. It was found necessary during the study to add sodium or ammonium nitrate in the feed in order to suppress formation of hydrogen sulfide arising from high sulfates contained in the raw wastes. Up to 500 mg/l nitrate salts were added. Anaerobic lagooning studies were carried out at ambient temperatures around 22°C, but also at 15°, 10°, and 5°C.

The pilot anaerobic lagoon was operated for a continuous period of 54 weeks. For the first 16 weeks, the lagoon was maintained at ambient temperatures of 20-25°C. The BOD results showed steadily increasing BOD in the lagoon effluent but, near the end of the 16 weeks, equilibrium conditions were being approached with an effluent BOD around 1,100 to 1,200 mg/l. The pH level held in the range of 6.8 to 7.2. Howe et. al. (51) state that a balanced anaerobic environment is necessary. In the initial phases of anaerobic stabilization, complex organic compounds are converted to volatile acids. Concurrently, organic nitrogen materials must be converted to ammonia in order to neutralize the excess volatile acids in solution. This also prevents occurrence of drastic pH changes in the anaerobic basin.

Control temperatures within the anaerobic basin were then dropped to 15°C and maintained at this level from the 16th week through about the 30th week. The effluent BOD tended to stabilize around 1,200 mg/l, and BOD reductions were determined to be at least 80 percent as specified under the study objectives. Volatile acids (as acetic) and alkalinity (as $CaCO_3$) stabilized at around 1,000 mg/l and 2,200 mg/l, respectively. Unfortunately, at about the 28th week, process changes in the CSC plant caused a drastic shift in the composition of the feed to the pilot lagoon. The ammonium ion content dropped off appreciably and was substituted for by up to 25,000 mg/l sodium ions. The balanced anaerobic environment was significantly disturbed from the 30th week through the 37th week. Volatile acids, alkalinity and BOD increased to respective peaks of 2,300 mg/l, 3,800 mg/l and 2,500 mg/l. Acclimation of the system to the changed feed was noted around the 37th week, and at this point temperature was dropped to 10°C and subsequently to 5°C. At the lower temperatures of 10°C and 5°C, effluent BOD increased markedly but leveled off to around 4,000 mg/l. This corresponded to a BOD reduction through the system of about 60 percent based upon an incoming feed concentration of 10,000 mg/l BOD. Alkalinity and volatile acid concentrations stabilized in the range of 3,700-4,300 mg/l for alkalinity, and 2,200 to 2,700 mg/l for volatile acids. Fairly large amounts of settleable solids were observed during operation of the experimental lagoon.

A full-scale 8 hectare (20 acre) anaerobic lagoon was reportedly completed sometime around 1962-1963. The maximum depth of this lagoon was reportedly only 1.2 m (4 ft) which is somewhat surprising. A small forebay area was designed at the influent end of the lagoon specifically intended for settling of gross solids. Retention time of wastes in the lagoon was calculated as 220 days. The Company indicated that lagoon temperatures of 5°C or below were not expected over long periods. Based upon the pilot plant studies and full-system design, CSC personnel predicted a somewhat optimistic 80 percent reduction of BOD. The Company expected lagoon effluent loads to the River of no more than 820 kg (1,800 lb) BOD/day (51).

Fermentation Waste Disposal by Spray Irrigation Year-Round

Woodley, chief environmental officer of CSC, provided a 1968 status report upon the Terre Haute pollution abatement facilities with special emphasis upon the waste spray irrigation system installed in 1965 (11). The latter system was designed to replace, at least in part, the anaerobic lagoon constructed previously. Woodley describes the overall picture at Terre Haute during 1965-1968 as follows:

1) Spray irrigation of fermentation wastewaters
2) Anaerobic lagoon system for chemical product wastewaters
3) Solids resulting from vacuum filters taken to sanitary landfill
4) Sanitary wastes discharged to city sewer system
5) Small pond for settling of sluiced bottom ash from the boilers at the power plant
6) Release of the remaining low concentration wastes to the Wabash River

The land application system started in August 1965 was principally intended for the treatment and disposal of low volume, high BOD fermentation-derived wastes. The spray system covered an available 150 hectares (372 acres) of land, but as of March 1968 only about 65 hectares (160 acres) had been put into actual use. Based upon operating experiences from August 1965 through March 1968, the Company contends that satisfactory waste treatment performance can be obtained during all weather conditions including wintertime temperatures in the minus 0°C range; furthermore continuous irrigation can be maintained even during times of severe flooding in the Wabash River valley. Over this two and one-half year period, the Company estimates that 6,500 kkg (14,300,000 lb) of raw waste BOD were "adequately-treated" and disposed of via the spray irrigation system. This bulk waste load equates to an average of 6,700 kg (14,800 lb) BOD/day which was a very sizeable increase over the raw waste loadings of the early 1960's. The disposal site is reasonably well protected by levees along the Wabash River and adjoining bottom areas.

The spray disposal site, located across the River from the CSC manufacturing plant, as of 1968 comprised roughly 100 active 0.4 hectare (one-acre) spray plots, 40 inactive 0.4 hectare (one-acre) spray plots, two 320 m^3 (85,000 gal.) earthen waste equalization basins, a 0.8 hectare (2-acre) anaerobic lagoon, an inactive lagoon of about 4 hectares (10 acres), and a refuse dumping area for mycelium and trash. The 8 hectare (20-acre) lagoon excavated in 1962-1963 was either subsequently abandoned, or more probably converted to the 0.8 hectare (2-acre) anaerobic pond and inactive lagoon as cited in the 1968 status report.

Fermentation wastes going to the spray irrigation site were reported as having BOD strengths as high as 64,700 mg/l. The land was generally sprayed 1.4 hectares (3 acres) (three consecutive plots) at a time, with any single plot sprayed continuously for 10 hours before resting.

The 10 hours of spreading at 340 l/min (90 gpm) amounted to around 200 m^3 (54,000 gal.) being applied to each spray plot. After dosing, the spray plots were rested two weeks or more until the next application. Calculations show a maximum daily application rate onto the spray irrigation fields of around 380 m^3/day (100,000 gpd). However, the long-term spray application rate probably averages closer to 230 to 260 m^3/day (60,000 to 70,000 gpd). About 4.9 kg/cm^2 (70 psi) pressure head was maintained both on the main header and lateral spray lines. Excessive runoff or ponding of spray plots caused individual plots to be taken out of service.

The accumulated record of fermentation waste disposal via the spray irrigation fields from August 5, 1965 through March 31, 1968 (almost 32 months) is summarized as follows:

Flow	-	214,300 m^3	(56,614,000 gal.)
BOD	-	6,471 kkg	(14,268,000 lb)
COD	-	14,800 kkg	(32,623,000 lb)
TSS	-	5,400 kkg	(11,976,000 lb)

Woodley comments that from the time the irrigation system was installed in 1965 through 1968 that the rates of waste application more or less tripled. Over this same period, the composite data show that the ratio of COD to BOD for these raw wastes averaged 2.29 and the corresponding TSS to BOD ratio was 0.84. A summary of monthly characteristics of raw wastes delivered to the land disposal site for the years of 1966 and 1967 is presented below. In reviewing these high waste strengths it is noted that no recovery of spent fermentation broths was practiced, by the company, as far as is known.

Table D-1
Monthly characteristics of CSC, Terre Haute Fermentation Wastes Discharged to the Spray Irrigation System, January 1966 to December 1967 (11)

Parameter	Range	Average
Flow (m^3/day)	150 to 320	250
Flow (gpd)	40,000 to 85,300	66,800
BOD (mg/l)	24,100 to 39,500	30,000
COD (mg/l)	47,000 to 90,000	67,000
TSS (mg/l)	5,900 to 55,000	26,000

A groundwater monitoring network was developed by CSC and was reported as showing no subsurface contamination. The land disposal system operates essentially via evaporation and adsorption. Transpiration is considered inconsequential since vegetation does not grow on the spray plots. It is reported however that revegetation does occur after suitable resting of the soils. Recontouring of the land surface was not recommended by the Company because of the costs involved. A significant number of problems were encountered in continued operation of the spray system, but by one means or another, the Company managed to alleviate these difficulties. This system was considered highly satisfactory towards solving the waste disposal needs of CSC. The report cautions that monitoring of groundwaters and the elimination or minimization of surface runoff or ponding are necessary requisites for a successful land application set-up (11).

Anaerobic Lagoon for Treatment of CSC Chemical Wastes, 1965-1971

A further report by Woodley and Brown in 1971 more fully describes the anaerobic lagoon system in receiving and treating the organic chemical wastes from the CSC, Terre Haute manufacturing facility (91). A small anaerobic lagoon of earthen construction was available with an approximate surface area of 0.8 hectares (2 acres) and a maximum depth of 1.5 m (5 ft). Monthly performance data collected of this lagoon over a five and one-half year period terminating in 1971, are shown in Table D-2:

Table D-2

Treatment of Chemical Plant Wastewaters by Anaerobic Lagooning
Commercial Solvents Corporation, Terre Haute, Ind.
July 1965 to March 1971 (91)

Parameter	Range	Average
Flow (gpd)	44,000 to 230,000	95,000
BOD (mg/l), influent	520 to 11,900	3,830
BOD (mg/l), effluent	130 to 5,220	1,240
BOD, % Removal	0 to 94	69
Volatile acids (mg/l)[a]	62 to 1,050	510
Alkalinity (mg/l)[a]	450 to 2,270	1,060
Nitrogen (mg/l)[a]	70 to 780	220
Phosphorous (mg/l)[a]	0 to 42	20
Hydrogen sulfide (mg/l)[a]	0 to 6	4
Sulfates (mg/l), influent	40 to 250	105
Sulfates (mg/l), effluent	0 to 230	40

[a] Refers to lagoon contents.

Close analysis of the 1965-1971 lagoon performance data showed that decreases in lagoon waste BOD removals were not reliably predicted by volatile acid and alkalinity levels, and their respective ratios. Periods of low BOD removals appeared to be more so related to low wintertime temperatures than to any other factor(s). Consequently, in September 1970 the anaerobic lagoon was deepened from 1.2 to 1.5 m (4 to 5 ft). The authors recommended that the depth of the lagoon should have been made 3.7 to 4.6 m (12 to 15 ft) in order to take full advantage of heating and anaerobic degradation.

The anaerobic lagoon through the late 1960's was receiving organic chemical processing wastes including specifically methylamines still bottoms; alkaterge condensate; amino butanol still bottoms; caustic washes of fermentation equipment; floor washings; and some sewage. The wastes were generally basic in composition tending to keep the pH of the lagoon contents in the 8.0 to 9.0 range. The wastes were thought to offer ample alkalinity for neutralization of the volatile acids formed in the lagoon.

Odor conditions around the anaerobic lagoon were reported of low magnitude attributed mostly to a "relatively" low amount of sulfates in the wastes entering the lagoon. It was indicated that if the sulfate content of the raw wastes could be kept below 100 mg/l, then no significant odors would arise. The anaerobic lagoon was operated on as low a sulfate feed as practicable. The Company contends that anaerobic lagoon treatment over 1965 to 1971 at the Terre Haute location was quite successful. Treatment efficiencies seemed to be more so controlled by temperature and pH rather than by the conventional volatile acids-alkalinity parameters. Efficiencies decreased markedly when the liquid wastewater temperatures fell below 17°C (63°F). The anaerobic lagoon was operated for six years at an average BOD loading around 2,000 kg/hectare (1,785 lb/acre) of pond surface or 0.16 kg/m^3 (10 lb/1,000 ft^3) of pond volume (91).

Recent Waste Handling and Abatement Procedures

As described previously in the Waste Sources section, the plant currently has three direct discharges to the Wabash River. The most concentrated wastes from the plant are disposed of by spray irrigation on land with no surface return to the River. Other concentrated wastes were conveyed to an anaerobic lagoon system for treatment before discharge to the River. This latter waste stream was connected to the City of Terre Haute municipal sewerage system in January 1974.

The lagoon system consisted of a 0.8-hectare (2-acre) and then a 8-hectare (20 acre) anaerobic lagoon during the 1960's. The latter evolved around 1971 into the 0.8 hectare (2-acre) anaerobic lagoon followed in series by a 5.7 to 6.5 hectare (14 to 16 acre) aerobic lagoon before final discharge to the River via Outfall 004. The aerobic lagoon was eventually abandoned in late 1973. Company design criteria on the anaerobic and aerobic lagoons as of September 1971 are presented in Table D-3.

Table D-3

Lagoon System Design Criteria

Criterion	Anaerobic Lagoon	Aerobic Lagoon
Area (hectares)	1.0	5.5
(acres)	2.5	13.5
Depth (m)	1.5	1.8
(ft)	5	6
Capacity (m^3)	15,520	98,400
(million gal.)	4.1	26.0
Detention Time (days)	27	176
Impressed BOD Load (kg/m^3)	0.15	--
(kg/hectare)	--	104
($lb/1,000\ ft^3$)	9.2	--
(lb/acre)	--	93
BOD Removal (percent)	75	80
TSS Removal (percent)	95	67

Company plans showed an average raw waste input to the lagoon system of 570 m^3/day (0.15 mgd) at 4,000 mg/l BOD and 3,000 mg/l TSS which equates to daily BOD and TSS loads of 2,270 kg (5,000 lb) and 1,700 kg (3,750 lb), respectively. Waste strengths leaving the anaerobic cell were expected to be 1,000 mg/l BOD and 150 mg/l TSS. Final effluent (Outfall 004) pumped from the terminal pond to the River was expected to contain in the order of 200 mg/l BOD and 50 mg/l TSS. Company projections indicated that effluent loadings leaving the lagoon system would approximate (250 lb) BOD and (62 lb) TSS daily. Overall system waste removals were predicted as 95 and 98 percent for BOD and TSS, respectively.

It is again mentioned that due to poor treatment performance, excessive odors, or other factors, the two pond system was essentially taken off line at the end of 1973. It is assumed these strong wastes amounting to about 570 m^3/day (150,000 gpd) with peaks up to 680 m^3/day (180,000 gpd), are now permanently connected to the city, and will not return to the River at any time in the foreseeable future. Apparently the city has willingly accepted this waste stream. Future pre-treatment requirements that may be imposed upon the Company as a result of this connection, are unclear as of this time. Actually the Company has two different tie-ins to the city, the 004 waste connection and a separate sanitary waste connection. Plant sanitary sewage is rated as 76 m^3/day (0.02 mgd), one-half going to the city in each of the above two lines.

The spray irrigation system was evaluated by EPA in June of 1974. The BOD of raw wastes received into the spray disposal system is in the range of 30,000 to 100,000 mg/l. The average flow rate through this system in 1974 has been around 340 m^3/day (90,000 gpd), with peak flows up to 760 m^3/day (200,000 gpd). Raw waste strengths have stayed roughly the same since the 1960's but flows have increased from 260 m^3/day (70,000 gpd) previously to 340 m^3/day (90,000 gpd) now. According to the Company, the spray system is currently operated 5 days a week and some 4 to 5 hours daily. CSC strives to keep the caustic level as low as possible in the system. Heavy rainfall through the first half of 1974 has led to unusual amounts of standing water in the disposal fields. Recycle pumps have not been able to keep up with the excess flows experienced.

Observation of the spray fields showed virtual absence of cover crops and apparent destruction of wooded stands. Four sprays are employed off a single movable header, each spray discharging over an effective ground surface of 0.4 hectare (1 acre). The sprays are moved to an adjacent location when the ground becomes saturated after a few days. Operation and maintenance of this spray system is said to require up to 8 persons nearly full time. Possibilities of appreciable odor, mosquito breeding and underground drainage to the Wabash River, if any, should receive more detailed evaluation in the future. Based upon previously reported waste characterization data for the spray irrigation system and a current wastewater volume of 340 m^3/day (90,000 gpd), raw waste loadings in the spray disposal network are estimated around 860 kg (19,000 lb) BOD, 19,700 kg (43,500 lb) COD, and 7,200 kg (15,900 lb) TSS daily.

WASTE LOADS

1967-1970 Waste Loads

In April 1971 the Company reported the following raw waste BOD loads for 1970:

System	Load	
	(kg/day)	(lb/day)
Spray Irrigation Disposal System	11,300	25,000
Anaerobic Lagoon	2,300	5,000
"Primary Solid Removal Facilities"	3,200	7,000
River Discharges 001, 002, 003 & 004	1,900	4,300
Total Raw Waste Load	18,700	41,300

The Company also reported average annual final BOD loads discharged for 1967-1970.

Year	Maximum Monthly (kg/day)	Maximum Monthly (lb/day)	Average Monthly (kg/day)	Average Monthly (lb/day)
1967	4,720	10,400	2,490	5,500
1968	2,760	6,080	1,790	3,950
1969	2,170	4,790	1,790	3,950
1970	2,390	5,260	1,950	4,300

From these tabulations, the Company claimed an overall 89.6 percent BOD reduction for 1970.

1972-1973 EPA Survey Results

Wastewater sampling surveys of the CSC plant were conducted by the Evansville, Indiana, field station of the USEPA during May 1972 and July 1973. The later survey found higher waste loads at all outfalls. In 1972 the total COD load discharged by Outfalls 001, 002 and 003 was less than 1,180 kg (2,600 lb)/day but the 1973 survey observed discharges totalling about 5,500 kg (12,100 lb)/day from the three outfalls. For Kjeldahl nitrogen, the May 1972 investigations gave 160 kg (360 lb)/day for discharges 001, 002 and 003, whereas the 1973 survey showed 240 kg (540 lb)/day. During the second study, all three outfalls demonstrated high fecal coliforms in excess of 1,000/100 ml. As an average of both surveys, total phosphorous concentrations for Outfalls 001, 002 and 003 were respectively 0.45 mg/l, 0.45 mg/l and 0.53 mg/l, which were not particularly high.

The EPA report prepared in connection with the May 1972 survey provided special critique upon BOD, COD, ammonia and Kjeldahl results for the CSC wastewaters. The report stated that 5-day BOD was a poor measurement parameter, especially for Outfall 003. Where the nitrogen content is relatively high compared to the carbonaceous demand, 5-day BOD values may result which are actually larger than COD values. In effect, nitrogenous BOD may comprise a significant portion of the BOD results obtained. Sample dilution seems to play a critical role in both the BOD and NOD for incubation periods of five or less days when working with pharmaceutical waste samples. The EPA report implied that 10 or 20-day BOD values would more accurately describe the CSC wastewaters than would 5-day BOD. Unknown and varying amounts of NOD could cause calculations on BOD removal efficiencies to be inaccurate.

The 1972 EPA Evansville report cites an instance where the 20-day BOD value was larger in magnitude than could be expected from the sum of TOC plus unoxidized Kjeldahl nitrogen. This was attributable to incomplete digestion of organic nitrogen compounds in the ammonia analytical procedures. The EPA Evansville laboratory obtained only a 40 percent efficiency in digestion of methylamine and only a 10 percent efficiency in digesting trimethylamine. The report recommends, with specific nitrogen compounds such as those manufactured by CSC, that the Company's efficiency in organic nitrogen digestion, for purposes of running the nitrogen analysis, should be explicitly stated.

Recent Company Waste Load Data

Monthly report sheets on pollution abatement routinely supplied by the Company to the State give extensive analysis of BOD loads for Outfalls 001, 002 and 003 and some data on BOD loads to the 004 waste handling system and to the spray irrigation disposal system. A summary of this monthly data is presented in Table D-4 covering the 20 month period from October 1972 through May 1974. The tabulation shows that the monthly raw waste loads varied from 9,300 kg (20,500 lb)/day BOD up to a maximum of 20,800 kg (45,800 lb)/day, averaging out at 13,900 kg (30,700 lb)/day. The same sheets show that the final BOD loads being discharged to the River aggregated for the 001, 002 and 003 outfalls (on a monthly basis) ranged from 500 to 2,200 kg (1,100 to 4,900 lb)/day, averaging some 1,250 kg (2,760 lb)/day. The Company for this 20 month period reported a combined discharge to the Wabash River averaging 27,300 m^3/day (7.22 mgd). The raw waste BOD load for the last 10 months averaged 13,900 kg (30,600 lb)/day, almost the same as the 20-month average. Overall BOD removal efficiencies varied from 87 to 96 percent, averaging 91.0 percent, in spite of the fact that 9 percent of the raw waste loads received no treatment. This data analysis shows somewhat higher BOD percentage removals compared to the 1967-1970 situation described previously, and also, 25-50 percent lower organic loads in the final effluents compared to the former period.

Information provided by Commercial Solvents Corporation in August 1974 indicates a BOD raw waste load into the spray disposal system around 8,800 kg (19,500 lb)/day, and a raw waste load via the old 004 waste line which is now going to the city of around 4,800 kg (10,500 lb) BOD/day. The first figure is believed too low and the second too high but nevertheless the two add up to 13,600 kg (30,000 lb) BOD/day which is extremely close to the raw waste load estimates abstracted from the Company's monthly report sheets. The long-term average raw waste load of the CSC plant has been taken as 14,100 kg (31,000 lb) BOD/day. The monthly report sheets from October 1972 through May 1974 enable characterization of the 001, 002 and 003 discharges as given in Table D-5. There was essentially no discharge from Outfall 004 for this period of record.

Table D-4

Summary of BOD Waste Load Data for Outfalls 001, 002 and 003
Commercial Solvents Corp., Terre Haute, Indiana
October 1972 - May 1974

Month	Flow		Raw Waste Load		Final Waste Load		BOD Removal
	(m^3/day)	(mgd)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(percent)
Oct. 72	27,400	7.24	10,700	23,700	1,400	3,080	87.0
Nov.	28,810	7.61	11,900	26,300	1,310	2,890	89.0
Dec.	28,810	7.61	10,900	28,900	1,310	2,890	90.0
Jan. 73	28,770	7.60	9,400	20,800	1,220	2,700	87.0
Feb.	26,570	7.02	9,300	20,500	1,120	2,460	88.0
March	25,510	6.74	10,300	22,600	1,130	2,490	89.0
April	25,740	6.80	16,900	37,200	1,580	3,490	90.6
May	26,800	7.08	16,500	36,300	1,090	2,400	93.4
June	28,280	7.47	17,400	38,300	1,220	2,680	93.0
July	27,250	7.20	11,800	26,100	1,240	2,720	89.6
Aug.	28,010	7.40	15,900	35,100	1,030	2,280	93.5
Sept.	28,770	7.60	15,400	33,900	1,510	3,320	90.2
Oct.	25,170	6.65	20,800	45,800	1,250	2,750	94.0
Nov.	26,500	7.00	13,600	30,000	1,490	3,290	89.0
Dec.	26,500	7.00	17,400	38,300	2,220	4,900	87.2
Jan. 74	25,590	6.76	19,800	43,700	1,490	3,290	92.5
Feb.	29,530	7.48	11,800	26,000	1,170	2,590	90.0
March	26,310	6.95	14,900	32,800	930	2,060	92.0
April	27.900	7.37	9,500	20,900	860	1,890	91.0
May	29,530	7.80	12,500	27,600	500	1,100	96.0
Average	27,330	7.22	13,900	30,700	1,250	2,760	90.6

Table D-5

Characteristics of Waste Discharges from Outfalls 001, 002 and 003 October 1972 - May 1974

Parameter		Outfall 001	Outfall 002	Outfall 003
Flow				
Average	(m^3/day)	2,760	11,960	12,600
	(mgd)	0.73	3.16	3.33
Range	(m^3/day)	1,140-4,620	11,000-13,200	10,300-14,600
	(mgd)	0.30-1.22	2.90-3.50	2.72-3.85
BOD				
Average	(mg/l)	29	37	63
	(kg/day)	84	400	770
	(lb/day)	185	880	1,690
Range	(mg/l)	13-101	20-116	22-96
	(kg/day)	19-319	230-1,300	280-1,280
	(lb/day)	42-704	500-2,860	620-2,820

Since the majority of the organic waste load discharged directly to the Wabash River from the CSC Plant is associated with Outfall 003, it is presumed that future waste abatement must focus on this particular outfall in preference to Outfalls 001 and 002. It is noted that the very frequent flooding of overflow weirs on Outfalls 002 and 003 represents a continuing problem which makes flow measurements impossible and sampling sometimes impracticable. It has been recommended that the Company find a solution to this prevailing compliance monitoring difficulty.

Partial data concerning COD loads in discharges 001, 002 and 003 over the period January through April 1974 was provided by CSC to the EPA. The derived average COD;BOD ratio of 3.80 and an associated TSS:BOD ratio of 0.70 were determined applicable to the waste stream being discharged to the city and to the River. These were compared with previously-reported organic and solids loads discharged to the spray disposal system. Accordingly, total average CSC plant raw waste loads potentially available for treatment and disposal roughly equate to 14,060 kg (31,000 lb) BOD/day, 33,600 kg (74,000 lb) COD/day, and 9,750 kg (21,500 lb) TSS/day. It is recognized that raw waste loads can vary significantly from month to month, principally depending upon the type and number of fermenter tanks dumped over a specified time period, the number of spoiled fermentation batches experienced, the degree of recovery, if any, of spent fermentation beers, the nature and degree of solvent losses, contamination in reactor and still bottoms released to the CSC waste disposal systems, and various other factors. Still bottoms are yet reported as going to the River in undefined quantities. Filtered-out fermentation mycelium, generally running about 20 percent solids content, are usually taken to landfill. This mycelium may amount to a few thousand pounds of BOD daily. This mycelium has not been added into the basic raw waste load at CSC. Its removal is either necessary or included under basic housekeeping procedures employed at a bulk pharmaceutical fermentation plant. Future attention must be given to waste equalization, and the elimination or removal of selected waste sources, spills, and surges within the CSC system.

DISCUSSION OF NPDES PERMIT CONDITIONS

Reservations have been expressed whether BOD can be properly run on CSC wastewaters. Consequently both BOD and COD limitations have been employed in the permit. Recovery of fermentation spent broths has been taken as the "minimum" equivalent acceptable treatment for fermentation wastes within the pharmaceutical industry, meaning a 95 percent or better reduction of BOD. Considering prevailing waste handling and treatment practices, the Best Practicable Control Technology Currently Available for the Terre Haute plant has been established as a 97.2 percent BOD reduction based upon current raw waste loads. At Terre Haute, it is estimated that fermentation activities roughly comprise 45 percent of the BOD raw waste loadings of 13,600 to 14,100 kg (30,000 to 31,000 lb) BOD daily. On the organic chemicals production side, a required minimum of 93.5 percent BOD reduction has been called for. The average daily and maximum daily BOD limitations specify 820 and 1,270 kg (1,480 and 2,800 lb)/day BOD respectively, to be achieved by 1976, as the total allowable organic loads from all CSC outfalls.

A COD reduction of 80 percent has been indicated in the proposed NPDES permit which equates to 6,350 kg (14,000 lb)/day COD as the average daily allowable value. However, both the 1971 CSC permit application and results of previous EPA sampling surveys show that 5,440 kg (12,000 lb) COD/day are consistently being achieved at the present time. The latter figure therefore establishes the controlling 1976 COD condition for this permit. With the types of waste control and treatment facilities envisioned at Terre Haute in the future, an overall 95 percent TSS removal based upon raw waste loads is expected. This yields an average daily limit of 500 kg (1,100 lb)/day TSS to be reached by 1976-1977. The limitations on BOD, COD and TSS in the permit will necessitate additional waste removals of zero to 60 percent over the next three or so years.

Excessive ammonia and organic nitrogen are present in the wastewaters from many bulk pharmaceutical manufacturing establishments. Oxidation of ammonia to nitrate nitrogen can theoretically consume about 4.6 parts of oxygen for each part of ammonia present in the wastewaters. This compares to only about 1.4 parts of oxygen necessary for each part of BOD. Organic nitrogen, correspondingly as for ammonia nitrogen, has a high DO demand for conversion into nitrates. Secondly, ammonia is decidedly toxic to fish and aquatic life under varying stream conditions. Thirdly, even moderate levels of unoxidized nitrogen can give distorted results in running the BOD test on industrial plant effluents. Additionally, ammonia and other organic nitrogenous compounds during chlorination serve to form chloramines and similar compounds which in turn are highly toxic to fishlife, impart off-tastes to water supplies, and have other undesirable side effects. In a series of recent industrial cases, not only has the critical need been shown for ammonia and total nitrogen reductions in wastewaters, but also available technology has been described to bring organic nitrogen-laden wastewaters down into the range of 10 to 20 mg/l. Because of the prevalence of quite high levels of ammonia and organic nitrogen in the bulk pharmaceuticals manufacturing industry, it has been recommended by 1976 that 25 mg/l ammonia nitrogen or less, shall be attained within the treated CSC process effluents. This recommendation has been incorporated under effluent limitations for the pharmaceuticals industry. For CSC, Terre Haute, average daily and maximum daily limitations on ammonia-N have been tentatively set at 73 kg (160 lb)/day and 145 kg (320 lb)/day, respectively, to be achieved by 1976-1977. EPA sampling results in 1972 showed an average total of 161 kg (355 lb)/day ammonia-N, and 39 kg (85 lb)/day organic-N in Outfalls 001, 002 and 003. EPA 1973 results demonstrated an average total of 145 kg (324 lb)/day ammonia-N and 117 kg (259 lb)/day organic-N within the three outfalls. Required future ammonia nitrogen reductions are in the range of 25 to 60 percent compared to present conditions.

The 1973 EPA survey found average chromium and zinc levels in Outfalls 001, 002 and 003 ranging up to 0.35 and 0.6 mg/l, respectively. Sulfides, oil and grease, and phenolics were present in amounts considered sufficient to warrant effluent limits. A sulfide limitation of 0.5 mg/l has been established for the future. Maximum allowable levels of phenolics and total chromium have been set at 0.25 mg/l for the average daily condition. The upper level of zinc has been set at 0.75 mg/l and oil/grease at 10 mg/l. Sulfates (90-290 mg/l) and alkalinity (165-1,500 mg/l) are quite high but no industry-wide limitations have been proposed for these parameters.

Methanol has been tested for in the past and, in May 1972, a value as high as 1,150 mg/l was recorded in the anaerobic treatment pond system. However, amounts of methanol and of methylamine, dimethylamine and trimethylamine were repeatedly less than 5 mg/l both in 1972 and 1973 for Outfalls 001, 002 and 003. No limitations have been established in the NPDES permit for the latter parameters.

Monitoring requirements were established for pesticides, chlorinated hydrocarbons and toxicity.

E-1-a

PHARMACEUTICAL INDUSTRY

CASE HISTORY E

MERCK & CO., INC., STONEWALL PLANT
ELKTON, VIRGINIA

(FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PLANT)

MERCK & CO., INC., STONEWALL PLANT, ELKTON, VIRGINIA
(FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PLANT)

BACKGROUND

The Stonewall Plant of Merck & Co., Inc., at Elkton, Va., on the South Fork of the Shenandoah River, was started around 1941. In the early 1950's, operations included fermentation, processing and the manufacture of synthesized medicinals consisting of antibiotics, vitamins and sulfa drugs. In the late 1950's manufactured products consisted of fine chemicals plus fermentation-derived ingredients including Vitamin B_1, Vitamin B_2, Vitamin B_{12}, Lysine, Streptomycin, Sulfaquinozaline, Nicarbazin, Glycamide and various feed supplements. Operations were broadly categorized as organic synthesis, fermentation, extraction and solvent recovery (66, 93).

Presently, the Stonewall installation is a moderate-sized bulk pharmaceutical manufacturing facility producing both human and animal medicinals consisting of antibiotics, vitamins, coccidiostats, steroids, amino acids, and feed supplements. Major products reported by the Company in December 1970 included three compounds essentially generated by fermentation: Cyanocobalamin, otherwise known as Vitamin B_{12}; the antibiotic, Streptomycin; and the amino acid, Lysine. Other products made primarily, if not entirely by organic synthesis reactions, included Riboflavin, also known as Vitamin B_2; Thiamine leading into Vitamin B_1; the animal coccidiostats Sulfaquinoxaline, "Nicarbazin," and "Amprolium;" and the chemical intermediate Aminothiazole. Chemical restructuring of modified penicillin forms is also thought to be conducted at this installation. Recent data provided by the Company indicates that Stonewall manufactures from 12 to 24 different "bulk" chemicals and some 40 to 60 intermediate chemicals. Approximately 30 different solvents are used for extraction and/or overall processing. Specific product data could not be obtained from the Company. The installation operates 24 hours per day, 7 days a week and current employment is between 500 and 550 persons.

The South Fork of the Shenandoah River is associated with some of the more demanding water quality criteria in the State of Virginia since the waters are classified as Mountainous Zone waters and the town of Shenandoah withdraws its public water supply downstream of Merck. The South Fork is classified for use as domestic water supply, agricultural water supply, livestock watering, for propagation of fish and aquatic life, and for boating and aesthetic enjoyment.

PROCESSES

The Stonewall Plant is a major fermentation facility. There are approximately two dozen fermenters on site ranging from small through "standard" (37,900 to 64,400 l, or 10,000 to 17,000 gal.) up to very large in size. The very large fermentation tanks can have serious impact on the waste treatment system when dumped.

In December 1970, the Company indicated that all three cited fermentation products were extracted by adsorption of the active ingredient(s) onto ion exchange resins. Spent fermentation broths, from which the desired products have been removed, from the Vitamin B_{12}, Streptomycin and Lysine processes were all being directly released into the liquid waste collection system for ensuing biological treatment. The Vitamin B_{12} production is a whole broth process with soybean meal employed as one of the fermentation substrates. In most fermentation plants, after chemical recovery of the vitamins, the spent broth is usually dried and incorporated into animal feed supplements. However, this is not the case at the Stonewall Plant. Company personnel state that making broth up into animal feed supplements is not economically competitive. The fermentation broths are relatively liquefied with low suspended solids concentratons apparently discouraging mycelium filtration and the economical recovery of the stripped broths. No removal of mycelium by separate filtration is believed practiced and, consequentially, all of this material likely enters into the waste treatment plant.

Streptomycin and Vitamin B_{12} production are similar in some respects; the fermentation broths have nearly the same color and fermentation temperatures are similar.

It was observed that the contents of the equalization basin within the main treatment works were almost the same color as the broths inside the factory, reinforcing the conclusion that spent fermentation broths contribute heavily to raw waste loads at Stonewall.

The Company in their December 1970 report commented upon the production of steroids and animal feed supplements. Steroid products are considered a minor manufacturing line with processing consisting essentially of recrystallization and isolation of desired ingredients from previously-purchased semi-refined stocks. No wastes are reported produced other than floor washes and used solvents, the latter being primarily incinerated. The preparation of food supplements involves operations such as drum drying, blending, milling, screening and packaging. Waste streams include floor and equipment washings.

Organic chemical products are synthesized from a wide spectrum of inorganic and organic raw materials. Waste streams generated from these manufacturing sectors include mother liquors, cake washes, reactor residues, column and extractor spent solutions, aqueous distillates, floor and equipment washings and a wide variety of miscellaneous discard lines. The majority of these streams end up in the waste treatment works.

Solvents such as methanol, ethanol, acetone et.al., used in various extraction and stripping operations, are mostly collected and recovered at a centralized solvent recovery station for reuse in processing. Other solvent recovery is exercised at individual process stations. The

Company could not provide the EPA with the efficiency of these operations. Tarry still botttoms are separately collected and trucked from the plant site, presumably to landfill.

The Company emphasized the high variability of product mix possible at any single time. Large amounts of salts are apparently utilized within processing as evidenced by high inorganic loads in the wastewaters.

Plant personnel remarked that new surface condensers are mainly in use, with only two or three barometric condensers allegedly remaining within the manufacturing plants.

The Company reports that approximately one-half of the liquid process wastes and raw waste loads originate from fermentation; the other half comes from organic chemical synthesis operations.

All intake water supply, approximately 37,900 to 41,700 m^3/day (10 to 11 mgd), is obtained from Company well fields; the ground water is quite cool at about 12.8 °C (55°F). Water for cooling and industrial processing receives only chlorination. Water for the boilers and associated needs is treated by softening, filtration and deaeration. The potable supply is chlorinated and filtered.

Plant power is supplied by four boilers: three on coal and the fourth on No. 5 fuel oil.

Air pollution control devices are minimal up to the present time. However, water scrubbing is believed utilized on the spent air streams from Vitamin B_1 process operations.

The quality control lab was visited during March 1974. Colonies of small animal species, mostly rabbits and white mice, are routinely maintained. The animals are used for acute toxicity testing and occasionally for oral toxicity testing. A type of bacterial bioassay is conducted which measures the rate and effectiveness of bacterial die-away when Streptomycin is introduced into the test.

WASTE TREATMENT AND CONTROL

Early Waste Treatment

In the early 1950's the Stonewall Plant contributed a total waste load of 454 to 2,270 kg (1,000 to 5,000 lb) BOD/day to the River. Strong wastes including fermentation process spent liquors, fine chemical mother liquors, and various washes, concentrates and still residues having a BOD strength in the range of 3,000 to 100,000 mg/l were evaporated to a concentrated solution which was then incinerated. "Weak" liquid wastes were discharged to a common sewer and the combined effluents subjected to equalization, oil skimming and sludge removal within two consecutive basins prior to being discharged to the River. Spent cooling waters and "jet" discharges of "negligible" BOD flowed into the second skimming basin and then to the River. Sanitary wastes were settled in a clarigester, chlorinated and then discharged to the second skimming basin. Solid wastes and trash were collected and incinerated.

In the early 1950's, production was rapidly expanding, and laboratory and pilot plant studies were conducted on biological treatment, particularly trickling filtration, in order to provide increased flexibility in waste disposal, to improve the effluent to the River, to "decrease operating costs" for waste treatment, and to minimize the possibility of air pollution from incineration of wastes within the then-existing system (93). The stated objectives were at that time "to devise a simplified scheme of waste treatment which would require considerably less supervision and would eliminate the complex system of wastes segregation and handling." Ironically, these objectives are now receiving serious reconsideration in the light of current regulations and requirements.

The initial pilot-scale trickling filter unit installed in October 1951, was studied with respect to treating fermentation wastes. The filter was operated for nine weeks at recirculation ratios of 12:1 and 18:1. Strength of the feed material approximated 3,500 to 4,100 mg/l BOD. Average BOD reductions were 66 to 78 percent. The toxicity threshold value of the filter effluent, determined with Daphnia magna was as low as 0.65 percent. Filter growths were very heavy on occasion and the potential for ponding and odors was present. A single trickling filter was judged insufficient for adequate BOD removal. Heavy filter growths and high recycling rates commensurate with high operating costs, were also judged unfavorable from the Company standpoint. The decision was made to dilute the fermentation liquors with the relatively weaker general plant wastes and treat the mixture on two filters in series at comparatively low recirculation rates (93).

Two pilot-scale filters were set up in series with intermediate and final clarifiers treating mixed fermentation and general plant wastes. Recycle ratios of 3:1 and 5:1 were employed around the two filters. Average BOD of the raw feed was in the range of 700 to 780 mg/l. Overall BOD reductions were 84 to 87 percent, and the average effluent toxicity thresholds were 80 percent to 100 percent.

Next, the strong process wastes previously incinerated, having an average BOD of 30,000 mg/l, were brought into the trickling filter pilot plant. Evaporation and incineration of these wastes were equated with unacceptably high operating costs by the Company. The mixture of spent fermentation liquors, general plant wastes and the strong process wastes approximated a BOD of 900 mg/l. The two-stage filter setup was operated for three months at a recycle ratio of 5:1 with average BOD loadings of 0.98 kg BOD/m^3 (1.65 lb/yd^3)/day on the primary filter, and 0.39 kg BOD/m^3 (0.65 lb/yd^3)/day on the secondary filter. Overall BOD reduction averaged 84 percent with an effluent BOD of 135 mg/l. The toxicity threshold determined with Daphnia magna was 25 to 50 percent on the final effluents compared to a threshold value of less than 0.1 percent on the raw mixed feed.

The reported results on the pilot trickling filter studies ended with consideration of a preliminary full scale design. The tentative layout comprised three trickling filters and two clarifiers. Two of the filters and one of the clarifiers would constitute the primary treatment stage, whereas the third filter followed by a clarifier were intended to comprise the secondary treatment stage. Design loading on the two primary filters was given as 0.9 kg BOD/m^3 (1.5 lb/yd^3)/day, and the estimated loading on the secondary filter was cited as 0.8 kg BOD/m^3 (1.35 lb/yd^3)/day. An overall BOD reduction of 80 percent was projected. Disposal of some 45 m^3 (12,000 gal.) of sludge daily was expected to be made onto adjoining cultivated lands.

Other Merck & Co. investigations in the early 1950's involved filtration and incineration studies on trickling filter sludges and also anaerobic digestion and land disposal of these sludges. Equipment costs were found to be too high for filtration and incineration. Hydrogen sulfide problems and other complications were associated with anaerobic digestion. Summertime disposal of sludges onto tilled soils showed acceptable rates of application up to 1.6 l/m^2 (0.04 gal./ft^2). Wintertime studies comprised surface dosing of soils with the sludges for up to four months. Some odor and fly problems were evident with the onset of warm weather but were eliminated when cultivation was resumed. The same surface dosing rate was judged satisfactory for the winter months (93). These early practices at the Stonewall Plant are not considered the best for handling and treating pharmaceutical wastes in view of current-day technology.

Waste Treatment in the Late 1950's

The waste treatment system changed appreciably by the late 1950's (66). Plant effluents essentially comprised three separate streams.

1) Some 26,500 m^3/day (7 mgd) of reportedly uncontaminated waters, containing spent cooling flows and unknown source contributions, which were discharged more or less directly to the River.

2) Approximately 76 m^3/day (20,000 gpd) of sanitary sewage were collected in an individual system and received primary and secondary treatment.

3) Chemical wastes made up of strong organics and spent fermentation broths, predominately acidic in nature, were directed into the main treatment works. These strong chemical wastes had a volume of 4,730 to 5,680 m^3/day (1.25 to 1.5 mgd) and were characterized by a BOD of 1,500 to 1,900 mg/l; COD of 3,000 to 3,500 mg/l; TSS of 500 to 1,000 mg/l; and pH levels varying from 1.0 to 11.0.

Liquid chemical wastes entered the main treatment plant through a bar screen and mechanical grit and trash removal unit and then flowed into an equalization basin which retained the wastes for 5 to 6 hr. Floating immiscibles were removed by a mechanical skimmer and periodically burned. Effluent from the equalization basin was neutralized to around pH 7.0, combined with the sanitary effluent which had received primary treatment in a 6.7 m (22 ft) diameter by 5.5 m (18 ft) deep clarigester, and sent to secondary treatment. Settled solids in the equalization basin were pumped to the sludge stabilization basin described below. The digested solids from the clarigester were periodically taken to sand filters with the filtrates returned to the clarigester.

Secondary treatment consisted of activated sludge aeration followed by two trickling filters in parallel. The combined flows cited above entered the mixed liquor activated sludge rectangular basin providing 4 hr waste retention. This basin overflowed into a flotation chamber where separation of solids was made. Part of the solids was returned to the aeration basin and the remainder pumped to an aerobic sludge holding chamber. The underflows from the flotation unit were released into a wet well serving two large trickling filters in parallel. Effluents from the filters were passed to a splitter box which divided the flow either for recycle or to a final settler. A recirculation ratio of about 7:1 was maintained. Sludge was removed from the clarifier into a sludge thickening tank. Clarified effluents from the final settler were combined with the untreated cooling water stream for final discharge to the South Fork of the Shenandoah River (66).

Settled solids from the chemical waste equalization basin, part of the solids from the flotation chamber and thickened sludge from the clarifier following the trickling filters were collected in aerobic sludge holding chamber where air was added and sludge stabilization effected prior to the sludge being trucked and disposed of onto Company lands. Capacity of the sludge stabilization basin was reported as 908 m^3 (240,000 gal.), sufficient to provide about 5 days of sludge holding and stabilization. Apparently excess sludges were also being taken from the flotation sludge collection box directly to land disposal.

Recent Waste Handling and Treatment Practices, 1970 through 1974

EPA, NFIC-Denver was requested by Region III in 1974 to prepare a

NPDES discharge permit for the Stonewall Plant. Consequently NFIC-Denver visited the Elkton, Va., manufacturing facility on March 13, 1974, to obtain an update on processing and waste control and treatment practices. This same plant had been previously inspected and evaluated by NFIC-D on July 7, 1972.

In May of 1970 a roughing biofilter, 18 m (60 ft) in diameter by 6.6 m (21.5 ft) high and containing 1680 m^3 (60,000 ft^3) of filtration media, was added to the existing Merck treatment works comprising the first stage of a three-stage bio-oxidation system ahead of the activated sludge and the trickling filter treatment phases. The biofilter was provided with recycling ratio capability of up to 6:1. The Company, in their December 1970 written presentation to the State of Virginia, reported an expected raw waste load of around 18,100 kg BOD (40,000 lb)/day. The final effluents, including the treated industrial and sanitary wastes and the untreated cooling waters, were reported as having the following characteristics:

Flow - 30,300 to 45,400 m^3/day (8 to 12 mgd)
BOD - 35 to 100 mg/l and 1540 to 3060 kg (3,400 to 6,750 lb)/day
COD - 250 to 375 mg/l
TSS - 40 to 100 mg/l
pH - 6.5 to 8.0

They indicated that their treatment plant would reduce BOD loads by at least 90 percent.

Except for the roughing biofilter, the Stonewall waste treatment works has not changed significantly in recent years.

The current waste treatment works is essentially a three-stage biological system for handling process and sanitary wastewaters. It is considered somewhat marginal in view of the steadily decreasing organic removal efficiencies that have been demonstrated from 1972 through 1974. The treatment of process wastes basically includes:

> A "tritor" mechanical grit and trash removal unit installed within a concrete flumeway. Solids and grit are removed for burning. The associated bar screen receives automatic cleaning. Bypassing around this unit is highly probable.
>
> Equalization basin, 18 m (60 ft) in diameter by 4.6 m (15 ft) deep with a holding capacity of 1,190 m^3 (315,000 gal.) and providing 3 to 6 hr detention for process wastes. The pH in the equalization basin ranges from less than 1.0 to greater than 13.0. The rapid variation is frequently caused by dumping of fermenter tanks and the large quantities of caustic or acid

utilized in the fermentation purification and recovery processes. This basin is served with a 30 HP agitator for mixing of incoming raw wastes.

Equalized process wastes pass through a small neutralization basin of 73m^3 (19,400 gal.) capacity, providing about 20 minutes waste retention. Acid and caustic additions are automatically made, and the outgoing pH values are usually in the range of 6.5 to 8.5. The neutralization box is equipped with two 7.5 HP turbine agitators.

Neutralized wastes are lifted into a primary clarifier 18 m (60 ft) in diameter by 2.4 m (8 ft) deep giving about 2 hr flow detention. Floatables are skimmed off the top. Primary sludges are sent to the aerated sludge stabilization basin, while settled effluents are sent to the first stage of biological treatment.

Large roughing biofilter as described above. Effluents are sent to the activated sludge subsystem.

The activated sludge portion of the plant consists of activated sludge aeration chambers, froth tanks for the collection of excess foam off the aeration tanks, aerobic sludge digestion or stabilization basins, and a flotation unit to separate the activated sludge effluents from return activated sludge. Detention time in the primary activated sludge basins approximates 4 hr. Excess foam ends up in the aerobic digestion basins. The flotation unit is reported to provide about 3-4 percent solids concentration in the separated sludges. Excess activated sludge is routed to the sludge stabilization basins. The activated sludge basins receive oxygen via four 25 HP and four 50 HP sparged turbine agitators.

The aerated sludge digesters receive sludges from the primary settlers, from the secondary settlers (following the high-rate trickling filters), and also from the activated sludge flotation unit. After some 2 to 3 days of aerobic digestion, the "digested" sludges are generally passed through SWEECO screens, a pair of centrifuges, and the sludge residues are then taken to land disposal. Triton centrifuges were installed principally to reduce the volumes of final sludges handled and the land acreages required for solids disposal. Supernatants from the sludge centrifuges are returned to the main treatment plant.

Activated sludge effluents are pumped over two 46.6 m (153-ft) diameter high-rate trickling filters approximately 1.2 m (4-ft) deep arranged in parallel. The filters are capable of attaining a recycle ratio of 7.5 to 1 and operating at a hydraulic loading up to 131,000 m^3/hectare/day (14 mgad).

Trickling filter effluents are passed through a pair of 12 m (40 ft) diameter by 3 m (10 ft) deep final settlers arranged in parallel. Clarifier overflows are carried underground to the small retention pond located near the River into which all plant waters combine before ultimate release to the River. Stonewall provides no chlorination of final plant discharges. The retention pond is skimmed when conditions dictate. In July 1972, discharges from this pond to the river where observed as dark in color and turbid.

Sanitary sewage at Stonewall approximating 75.7 m^3/day (20,000 gpd) or less is passed through a grinder and then to a two-compartment clarigester. Flows from the clarigester enter the main process waste treatment works immediately following the neutralization basin. Periodically sanitary sludges are directed to "small" sand filter beds.

Final sludges from the treatment works leaving the centrifuges or the aerobic sludge stabilization basins are trucked and applied to 47 ha (120 acres) of Company-owned lands about 0.8 km (0.5 mi) from the main factory. The sludges are applied by spreading or irrigating. The fields receive liming, and the sludges are periodically harrowed and plowed under. Sludge application rates are thought to be about 100 cm (40 in.) annually and the Company reports no surface runoff from these fields. There have been some indications of localized odors from the sludge disposal fields.

Spent cooling, air conditioning and surface waters from the plant grounds bypass treatment but combine with the treated process waters in a small final retention pond just before ultimate discharge to the South Fork of the Shenandoah River. Dilution is approximately 7 to 1, i.e. volume of cooling water plus treated process stream divided by volume of process water stream. Past data shows 3780 to 4920 m^3/day (1.0 to 1.3 mgd) process wastes vs. 27,200 to 32,200 m^3/day (7.2 to 8.5 mgd) of composite cooling water-surface runoff streams. Stonewall has no cooling towers to permit any significant reuse of spent cooling waters. Opportunities for process wastes, solvents and/or other incompletely-treated wastes bypassing treatment and intercepting the cooling and storm drains are judged reasonably probable.

In January 1972, the EPA requested Merck to submit a Spill Prevention, Containment and Counter-Measure Plan. The Company receives raw materials primarily by tank car thereby necessitating a sound spill prevention plan. It is not known whether such plan has been yet submitted.

Merck recently indicated to the EPA that essentially no removal of nitrogen and phosphorous waste loads may be expected through the existing Stonewall waste treatment plant. As far back as May 1972, the State had notified the Company that sometime in the future, denitrification and phosphorous removal would likely be necessary. Ammonolysis, amination, alkylation, diazotization, coupling of amino groups and other organic synthesis processes conducted at Stonewall illustrate the prevailing use of nitrogenous compounds.

WASTE LOADS

Appropriate wastewater characterization data includes the NPDES discharge permit application of 1971-1972; results of an EPA field sampling survey conducted in February 1972; and BOD and COD analysis on the waste treatment system supplied by the Company to the EPA in April 1974. Taking the last source of information first, summaries have been prepared for sampling results of 1972, 1973 and 1974, and these are given respectively in Tables E-1, E-2 and E-3. These tables provide characterization of the raw wastes entering treatment, the spent cooling water stream, and the combined treated process plus cooling water discharges.

It is noted that data for each of the three years of record was collected at somewhat different times of the year. In spite of this, the annual BOD input load to the treatment system averaged 18,400 kg (40,500 lb)/day in 1972, which somewhat surprisingly decreased to 13,200 kg (29,050 lb)/day BOD in 1973, and further decreased to 10,600 kg (23,400 lb)/day during 1974. The COD/BOD ratio for the raw process wastes approximated 2:1. The raw process flow rate correspondingly dropped off from about 6,620 m^3/day (1.75 mgd) in 1972 to 4,050 m^3/day (1.07 mgd) in 1974. Since no other data of similar nature was obtained from the Company, no other is believed available. Based upon this data it is presumed that the average raw waste loads have declined to around 13,200 kg (29,000 lb)BOD/day and 26,300 kg (58,000 lb) COD/day. The NPDES discharge permit for Stonewall was accordingly set on these bases. Conversely, the volume of cooling water has steadily increased from about 22,700 m^3/day (6 mgd) in 1972 to approximately 32,200 m^3/day (8.50 mgd) in 1974. The data array demonstrates that the Company can maintain the cooling water stream at or below 4 mg/l BOD and 11 mg/l COD. These concentrations coupled with a 1974 average cooling water flow of 32,200 m^3/day (8.5 mgd), equate to daily loads of 159 kg (350 lb)/day BOD and 386 kg (850 lb)/day COD.

The most notable feature of the performance data is that waste removal efficiencies significantly dropped from 1972 through 1974. The treatment plant in early-1972 was removing some 95 percent of incoming BOD raw waste loads and about 80 percent of the incoming COD. These percentage removals are quite close to the treatment levels now expected and being written for pharmaceutical plant permits by the EPA. Unfortunately, treatment performance in 1974 fell to about 87 percent BOD removal and only about 53 percent COD reduction. From the Stonewall record, we readily observe that the plant in 1972 with considerably higher raw waste loads was achieving better treatment performance compared to 1973 and especially compared to 1974.

Table E-1
Waste Treatment Performance, Merck & Company
Stonewall Plant, Elkton, Va., Feb. 28 - April 9, 1972

	Equalization Basin Effluent (Raw Process Wastes)			Cooling Water (Untreated) Discharge			Total Plant Final Effluent, Treated Process Plus Cooling Water Discharges (Outfall 001)			Waste Reduction Efficiencies (Percent)	
	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	Treatment Plant	Overall
						WEEK 1					
Flow		6,760[a]	1.786[b]		20,400[a]	5.40[b]		27,300[a]	7.20[b]		
BOD	2,270	15,300	33,800	4.	91	200	27	725	1,600	95.9	95.3
COD	5,610	37,900	83,500	13	270	600	286	7,800	17,200	80.1	79.5
TSS							71	1,950	4,300		
TDS							812	2,210	48,800		
						WEEK 2					
Flow		6,670[a]	1.762[b]		12,600[a]	5.70[b]		28,400[a]	7.50[b]		
BOD	2,790	18,600	41,000	12	270	600	40	1,130	2,500	95.4	94.0
COD	5,580	37,200	81,900	36	770	1,700	295	8,350	18,400	79.6	78.0
TSS							46	1,310	2,900		
TDS							832	23,600	52,100		
						WEEK 3					
Flow		6,150[a]	1.624[b]		22,000[a]	5.80[b]		28,000[a]	7.40[b]		
BOD	2,960	18,200	40,100	8	180	400	32	910	2,000	96.0	95.1
COD	5,740	35,200	77,700	25	540	1,200	271	7,580	16,700	80.1	78.8
TSS							50	1,410	3,100		
TDS							834	23,400	51,500		
						WEEK 4					
Flow		6,660[a]	1.760[b]		21,200[a]	5.60[b]		28,000[a]	7.40[b]		
BOD	2,480	16,500	36,300	5	91	200	23	635	1,400	96.7	96.2
COD	5,510	36,700	80,800	15	317	700	254	7,120	15,700	81.4	80.7
TSS							37	1,040	2,300		
TDS							832	23,300	51,400		
						WEEK 5					
Flow		6,740[a]	1.780[b]		24,200[a]	6.40[b]		31,000[a]	8.20[b]		
BOD	2,520	17,000	37,400	7	180	400	33	1,040	2,300	94.9	93.9
COD	5,660	38,100	84,000	22	540	1,200	249	7,700	17,000	81.2	80.0
TSS							29	900	1,980		
TDS							791	24,500	54,100		
						WEEK 6					
Flow		6,810[a]	1.800[b]		28,400[a]	7.50[b]		35,200[a]	9.30[b]		
BOD	3,620	24,600	54,300	11	317	700	52	1,810	4,000	93.9	92.7
COD	5,310	36,200	79,700	32	910	2,000	276	9,710	21,400	75.7	73.8
TSS							60	2,130	4,700		
TDS							777	27,400	60,300		
						AVERAGES					
Flow		6,630[a]	1.752[b]		23,100[a]	6.10[b]		29,500[a]	7.80[b]		
BOD		18,400	40,500		190	420		1,040	2,300	95.5	94.5
COD		36,900	81,300		560	1,230		8,030	17,700	79.7	78.5
TSS								1,450	3,200		
TDS								24,000	53,000		

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a/ Flow in m^3/day.
b/ Flow in mgd.

Table E-2
Waste Treatment Performance, Merck & Company
Stonewall Plant, Elkton, VA., Sept. 10 - Oct. 21, 1973

	Equalization Basin Effluent (Raw Process Wastes)			Cooling Water (Untreated) Discharges			Total Plant Final Effluent, Treated Process Plus Cooling Water Discharges (Outfall 001)			Waste Reduction Efficiencies (Percent)	
	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	Treatment Plant	Overall
						WEEK 1					
Flow		4,470[a]	1.180[b]		27,300[a]	7.20[b]		31,800[a]	8.40[b]		
BOD	2,970	13,200	29,200	2	45	100	31	998	2,200	92.8	92.5
COD	5,550	24,800	54,600	6	180	400	228	726	16,000	71.4	70.9
TSS							55	1,750	3,860		
TDS							790	25,100	55,400		
						WEEK 2					
Flow		5,860[a]	1.292[b]		25,700[a]	6.80[b]		30,700[a]	8.10[b]		
BOD	2,850	13,900	30,700	3	91	200	42	1,270	2,800	91.5	90.9
COD	5,570	27,200	59,900	9	227	500	283	8,660	19,100	68.9	68.4
TSS							58	1,780	3,920		
TDS							805	24,700	54,400		
						WEEK 3					
Flow		4,700[a]	1.243[b]		26,100[a]	6.90[b]		30,700[a]	8.10[b]		
BOD	2,760	13,000	28,600	3	91	200	28	860	1,900	94.1	93.4
COD	5,480	25,700	56,700	8	227	500	267	8,160	18,000	69.1	68.5
TSS							30	920	2,030		
TDS							883	27,100	59,700		
						WEEK 4					
Flow		4,890[a]	1.293[b]		25,000[a]	6.60[b]		29,900[a]	7.90[b]		
BOD	2,600	12,700	28,000	4	91	200	30	1,410	3,100	89.6	89.0
COD	5,710	27,900	61,600	11	270	600	238	8,610	19,000	70.1	69.5
TSS							30	910	2,000		
TDS							886	26,500	58,400		
						WEEK 5					
Flow		4,640[a]	1.227[b]		25,700[a]	6.80[b]		30,300[a]	8.00[b]		
BOD	2,760	12,800	28,200	3	91	200	34	1,040	2,300	92.6	91.9
COD	5,790	26,800	59,200	8	227	500	251	7,580	16,700	72.6	72.0
TSS							39	1,180	2,600		
TDS							834	25,300	55,700		
						WEEK 6					
Flow		4,250[a]	1.124[b]		32,900[a]	8.70[b]		37,100[a]	9.80[b]		
BOD	3,160	13,400	29,600	3	91	200	18	680	1,500	95.6	95.0
COD	5,810	24,700	54,400	9	320	700	233	8,610	19,000	66.4	65.5
TSS							25	925	2,040		
TDS							860	31,900	70,300		
						AVERAGES					
Flow		4,660[a]	1.23[b]		27,250[a]	7.20[b]		31,800[a]	8.40[b]		
BOD		13,200	29,050		91	200		875	1,930	92.7	92.1
COD		26,200	57,700		240	530		8,160	18,000	69.8	69.1
TSS								1,220	2,700		
TDS								26,800	59,000		

[a] Flow in m^3/day.
[b] Flow in mgd.

Table E-3

Waste Treatment Performance, Merck & Company
Stonewall Plant, Elkton, Va., Jan. 21 - March 3, 1974

	Equalization Basin Effluent (Raw Process Wastes)			Cooling Water (Untreated) Discharges			Total Plant Final Effluent, Treated Process Plus Cooling Water Discharges (Outfall 001)			Waste Reduction Efficiencies (Percent)	
	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	Treatment Plant	Overall
WEEK 1											
Flow		3,510[a]	0.926[b]		32,900[a]	8.70[b]		36,300[a]	9.60[b]		
BOD	2,048	7,170	15,800	15	500	1,100	36	1,310	2,900	88.6	82.8
COD	5,074	17,800	39,200	44	1,450	3,200	305	11,100	24,400	45.9	42.5
TSS							38	1,380	3,044		
TDS							810	29,400	64,900		
WEEK 2											
Flow		3,840[a]	1.014[b]		36,000[a]	9.50[b]		39,700[a]	10.50[b]		
BOD	2,518	9,660	21,300	5	180	400	44	1,770	3,900	83.6	82.0
COD	5,761	22,100	48,700	16	590	1,300	326	12,900	28,500	44.1	43.0
TSS							31	1,230	2,720		
TDS							829	32,900	72,600		
WEEK 3											
Flow		4,040[a]	1.112[b]		34,400[a]	9.10[b]		38,600[a]	10.20[b]		
BOD	2,551	10,700	23,600	5	180	400	41	1,590	3,500	86.9	85.4
COD	5,894	24,800	54,600	14	500	1,100	322	12,400	27,400	51.8	50.8
TSS							55	2,120	4,680		
TDS							901	34,800	76,700		
WEEK 4											
Flow		4,040[a]	1.067[b]		35,200[a]	9.30[b]		39,400[a]	10.40[b]		
BOD	2,647	10,700	23,500	4	136	300	30	1,180	2,600	90.2	89.1
COD	5,691	23,000	50,600	14	410	900	277	10,900	24,000	54.3	53.4
TSS							28	1,100	2,430		
TDS							840	33,100	72,900		
WEEK 5											
Flow		4,300[a]	1.171[b]		26,900[a]	7.10[b]		31,000[a]	8.20[b]		
BOD	2,432	10,400	23,000	3	91	200	41	1,270	2,800	88.7	87.9
COD	5,411	23,200	51,200	8	227	500	300	9,300	20,500	60.9	60.3
TSS							54	1,400	3,700		
TDS							855	22,100	58,500		
WEEK 6											
Flow		4,430[a]	1.171[b]		26,900[a]	7.10[b]		31,400[a]	8.30[b]		
BOD	3,378	15,000	33,000	5	136	300	40	1,270	2,800	92.4	91.6
COD	6,169	31,400	69,200	14	376	830	313	980	21,600	65.0	64.4
TSS							41	1,080	2,840		
TDS							836	26,300	57,900		
AVERAGES											
Flow		4,050[a]	1.071[b]		32,170[a]	8.50[b]		36,070[a]	9.53[b]		
COD		23,000	50,800		590	1,300		11,100	24,400	53.7	52.4
TSS								1,470	3,240		
TDS								30,500	67,300		

[a] Flow in m^3/day.
[b] Flow in mgd.

From the 1972-1974 data on TSS and TDS, it appears that solids in the final combined effluents have remained fairly constant over this particular period. The slight rise in TDS loads is believed attributable primarily to greater amounts of cooling waters used in 1974 compared to 1973 and 1972, and not to increases in synthesized organic chemicals manufacturing. Because of sludge disposal problems, caustic soda is used in neutralization to minimize sludge volumes, but in turn causes increase in TDS effluent loads. There was no data available on TSS raw waste loads. However, due to the "soluble" nature of this type of waste, TSS input loads are expected to be considerably lower than corresponding BOD and COD. Nevertheless the effluent TSS loads demonstrate that improved suspended solids separation and handling facilities are necessary at this plant.

Information contained in the Company NPDES permit application and results of the EPA sampling survey of February 1972 (both sources provide only limited data), indicate that the following waste parameters are of probable concern: nitrogen, phosphorous, chromium, phenolics, aluminum, lead, zinc, iron, copper, sulfides, cyanides and fecal coliforms.

DISCUSSION OF NPDES DISCHARGE PERMIT

Comparing future required procedures at Stonewall with the overall industry, the NPDES discharge permit has been predicated upon a 96-97 percent BOD removal for fermentation wastes and a minimum of 93 percent reduction of BOD coming from synthesized organic chemicals manufacturing. An 80-82 percent COD reduction has been additionally called for. These reductions are equivalent to loadings of 612 kg (1,350 lb)/day for BOD and 4990 kg (11,000 lb)/day for COD on an average daily basis. The past data on raw waste loads are important, and any possible substantiation of higher waste loads are important, and any possible substantiation of higher waste loads by the Company would require full documentation. If 1974 raw waste loads had been used as the base for effluent limitations (which was not done) much lower allowable loads would have been obtained. Average daily future TSS limits have been set at 590 kg (1,300 lb)/day, but some storm run-off may need to be removed from the waste collection system in order to reach this level. The above load limitations have been based upon recommended process load treatment plus cooling water loads to be expected from the plant when exercising a high degree of waste source control on the cooling water system.

Tentative limits were established for chromium, phenolics, zinc, iron, sulfides and fecal coliforms which are respectively given as 0.25 mg/l, 0.25 mg/l, 0.5 mg/l, 1.0 mg/l, 0.5 mg/l, and 200 organisms/100 ml. Sulfide limits are imposed because of the high levels of sulfates in pharmaceutical wastes. These recommended limits have been calculated upon what other industrial categories have been required to achieve with their process waste effluents alone. For Stonewall, the applicable flow for these concentration limits has been taken as 37,800 m^3/day (10.0 mgd). This represents process flows plus cooling water volumes. Additionally the State of Virginia has imposed a temperature limit of 24°C (75°F) upon the final effluents.

Based upon nitrogen removal technology explained elsewhere in this report and due to serious impacts of nitrogenous wastes upon water quality, specified nitrogen removal recommendations have been made in the NPDES permit. The past record shows that substantial amounts of ammonia and organic nitrogen are present in the wastewaters. Ammonium salts were previously reported as used in waste neutralization which significantly increased the nitrogen content of the effluents. Hopefully this practice has been discontinued. The Company permit application reported the combined treated process plus cooling water streams as containing 41 mg/l ammonia N and 54 mg/l Kjeldahl N, which are respectively equivalent to 1540 kg/day (3,400 lb)/day and 2000 kg/day (4,400 lb)/day. The process wastes per se are calculated to contain around 350-400 mg/l Kjeldahl nitrogen, the large part of which is ammonia N. Process waste streams have been determined as amenable to nitrogen recovery, in-plant control and/or treatment, if necessary. The proposed NPDES permit specified that 20-25 mg/l ammonia N shall be attained in the future in the treated process effluents. Phosphorous levels will be monitored in the present permit but will ultimately require more serious attention.

F-1

PHARMACEUTICAL INDUSTRY

CASE HISTORY F

MERCK AND CO., INC., CHEROKEE PLANT
DANVILLE, PENNSYLVANIA

(FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PLANT)

MERCK AND CO., INC., CHEROKEE PLANT, DANVILLE, PENNSYLVANIA
(FERMENTATION/SYNTHESIZED ORGANIC CHEMICALS PLANT)

BACKGROUND

The Cherokee Plant is a multi-product bulk pharmaceuticals manufacturing facility of medium size. However, considerable production expansion will be completed by 1975-1976. Current employment is 400 to 500 persons and operations are continuous, 24 hours per day, 7 days a week. The Danville complex, situated on the North Branch of the Susquehanna River, was once the site of a World War II government defense installation. Activities starting around 1944-1945 were directed to the manufacturing of hexamines used as raw materials in the production of explosives. Explosives were subsequently replaced by mono-sodium glutamate (MSG) and other chemicals. In 1969, MSG was in turn phased out and replaced by other products. Dryden et. al. (20) reported upon early waste handling and treatment experiences at the Cherokee Plant in the initial years of the 1950's, and the results of their study are summarized in a later section.

In the early 1950's the plant was, and still is, a fermentation and fine chemicals production facility. At that time, principal products included various antibiotics obtained by fermentation means, synthetic vitamins and cortisone. The first extensive waste treatment facilities at this location consisted of neutralization, waste equalization, alum treatment and attendant sludge handling and disposal. It quickly became obvious that additional treatment was necessary. The report by Dryden et. al. in 1956 described pilot plant investigations on the trickling filter and activated sludge processes eventually leading to a full-scale activated sludge treatment works in the late 1950's.

A number of bulk antibiotics and synthesized organic compounds are currently manufactured, plus a series of chemical intermediates. Data submitted by the Company in 1971 on the NPDES permit application refers to available processes for the manufacture of various antibiotics (mainly penicillin and its modified forms); the production of vitamins, largely niacin (nicotinic acid); steroid chemicals; and the processing of various industrial organic chemicals for the food and other industries, the principal compound being sorbitol. It is believed that the plant manufactures up to 30 to 40 different compounds. Currently plant activity is about evenly divided between fermentation and associated processing vs chemical intermediates, organic synthesized chemicals and their derivatives. This ratio will substantially change in 1975-1976 to 40:60 or possibly 35:65 as fermentation to organic synthesized chemicals. The change in 1975 involves the startup of large-scale "Aldomet" or 1-methyldopa production.

Of significant concern from the water pollution standpoint is the scheduled $60 million production expansion, primarily for the manufacture of "Aldomet". Additional organic waste loads plus unoxidized nitrogen loads to the river are receiving critical evaluation. Startup of Aldomet is expected around September 1975 and production increases are planned through 1976 and beyond.

Information regarding the Cherokee Plant of Merck and Co., Inc., at Danville, Pa. has been derived from 1) a single literature reference published in 1956 2) the 1971 NPDES permit application; 3) a plant visit made by EPA, NFIC-D to Danville on April 1, 1974; and 4) various detailed followups between the EPA and the Company in order to prepare the NPDES discharge permit for this installation.

PROCESSES

Processing schemes at the Cherokee Plant are not precisely known, but since sorbitol and niacin are two major organic synthesized products made by Merck, speculation may be offered on the particular manufacturing methods employed. From the literature, sorbitol is reported as generated from the catalytic hydrogenation of dextrose giving a 70 percent sorbitol in water solution. Sorbitol is not only sold to food processors but is also extensively employed as a precursor or starting material for Vitamin C manufacturing. In the above process, dissolved dextrose in water aided by liberal amounts of a nickel catalyst are fed into a continuous reactor under high pressure and heat and reacted with hydrogen. The sorbitol slurry is filtered and the clear sorbitol passed through ion exchange. Further purification is accomplished through activated carbon and the solution is concentrated in a continuous evaporator. Processing results in losses of nickel catalyst and activated carbon plus spent acids and alkalis from resin regeneration. There is indication of potential "cross-over" fermentation conducted by Danville in converting sorbitol to sorbol. Sorbol represents a subsequent possible by-product.

Niacin or nicotinic acid is an anti pellagra vitamin usually prepared from pyridine derivatives by processes such as the oxidation of β-picoline with air as the oxidizer and V_2O_5 as the catalyst. Potassium permanganate with electrolytic anode oxidation has also been employed. Nicotine and 2-methyl-5-ethyl pyridine have likewise in the past been oxidized to nicotinic acid.

Aldomet is known to come in at least two forms: as 1-methyldopa contained in tablets and as methyldopa hydrochloride prepared as an ester HCl injectable. Aldomet is considered one of the the more important anti-hypertensives available on the market recommended for patients with sustained moderate to severe hypertension, blood pressure and related ailments.

Methyldopa is generated both in the d-and l-isomeric forms. Conversion is attempted to the latter form since the activity of the compound is thought to reside almost entirely in the l-isomer. The chemical formula of the basic compound is $C_{10}H_{13}NO_4$. Alpha-methyldopa is otherwise known as α-methyl-3,4-dihydroxphenyl-alanine. Vanillin is one of the major base materials at the very beginning of the process. Large amounts of ammonia are believed employed in the main process. The l-α-, or α-methyldopa, is essentially synthesized from asymmetric intermediates. The main substrates used for the racemization and resolution processes (separation into respective optically active components) are likely dl-α-amino-α-vanillyl propionitrile and dl-α-acetamido-α-vanillyl propionitrile. The more recent techniques involve selective crystallization procedures in lieu of the more conventional resolution methods. Hydrolysis of the l-isomeric material concurrent with the newer techniques gives l-α-methyldopa in high yields. It is importantly noted that ensuing wastewaters because of liberal quantities of cyanides integrated in processing, must be passed through a cyanide destruction procedure at high pH before external release. Ammonia nitrogen waste loads are also significantly high.

WASTE TREATMENT AND CONTROL

Waste Sources

Plant water supply, averaging 7,520 to 9,520 m^3/day (20 to 25 mgd), is obtained from the Susquehanna River and passed through a preliminary settling pond. About 10 percent of the settled water is routed through an "iron-manganese removal system" that uses polyelectrolyte, alum and permanganate treatment. Cooling water does not receive iron-manganese treatment. Backwash sludges and filter washings from the water treatment plant are discharged to a small lagoon.

Primary plant boilers are coal fueled. Three of the four boilers are equipped with mechanical dust collectors. The sludge incinerator uses No. 2 fuel oil and is equipped with water spray condensation of gases and absorption via a packing column prior to final gaseous discharge. Bottom ash slurry from the boilers and scrubber effluent from the incinerator are discharged to the small lagoon receiving water treatment plant wastewaters.

Mycelium generated by fermentation activities is a major potential source of waste loads. Mycelium is recovered from some fermentation broths whereas it is not from others. Mycelium must necessarily be removed from penicillin fermentation beers, whereas this is not absolutely the case with many other antibiotics. Mycelium, if not separately filtered out and collected within the fermentation purification sector, becomes part of the raw waste load impressed upon the treatment plant. Mycelium that is reclaimed at 20-25 percent solids is admixed with partially-dewatered activated sludge for burning in a multiple-hearth incinerator. About 45 kkg (50 tons)/day of wet mycelium is said to be recovered at the Cherokee installation. Company personnel have indicated little interest in animal feed by-product recovery from fermentation operations.

According to information recently obtained from the Company, eight barometric condensers continue to discharge to the spent cooling water collection system. These units are a major source of waste loads discharged to this sewer system.

The plant has a centralized solvent recovery system. Unrecoverable solvents are collected at the solvent recovery station or otherwise segregated at their point of use and periodically disposed of via outside scavenger services. In spite of overall solvent recovery at this facility, contribution of organic raw waste loads due to "lost" solvents is thought to be fairly significant.

Wastewater streams generated by the Cherokee Plant in mid-1974 included 3,780 m^3/day (1.0 mgd) of process wastes, 380 m^3/day (0.1 mgd) of sanitary sewage and 71,900 to 83,300 m^3/day (19 to 22 mgd) of spent cooling water, boiler blowdown and miscellaneous wastewater streams. Sanitary sewage is discharged to the local municipal sewerage system. Process wastes are treated as described in the following section.

The volume of spent cooling water is surprisingly high as is the ratio of cooling water to process wastes which is in the range of 20 to 26:1. The spent cooling water, 95 percent of the Cherokee Plant effluent, is released "untreated" to the Susquehanna River.

Waste Treatment

Early Waste Treatment--Waste Treatment facilities in the early 1950's consisted of neutralization, equalization, alum treatment, and attendant sludge handling and disposal. Additional treatment became necessary and pilot plant studies were undertaken to evaluate treatment processes and determine design criteria.

Initially, a pilot-scale trickling filter setup was constructed to evaluate the treatability potential of the wastewaters (20). After a few weeks of operation, formidable problems became evident including an extremely prolific growth on the filters which could not be dislodged. Correspondingly, extreme ponding and drastic reductions in waste treatment efficiencies were experienced. At this point it was decided to analyze the activated sludge process as an alternate means of treatment, and this was done in an ensuing experimental program.

The laboratory study phase consisted of using a series of 5-liter batch aerators, 15 cm (6 in.) in diameter by 41 cm (16 in.) tall. Based upon varying sludge concentrations and BOD strengths of the raw waste feed into the aerators, the relation of BOD removal vs aeration time was adequately determined. From these tests, it was concluded that the activated sludge process was adaptable for treating the industrial wastewaters, a high degree of BOD removal could be obtained with reasonable aeration times, and further tests should be conducted at the pilot plant stage.

This activated sludge pilot plant was capable of handling flow rates up to 57 l/min (15 gpm). A series of test runs was conducted at various MLSS levels, feed rates and retention times. Removals of BOD varied from 50 to 93 percent. These runs demonstrated that an operationally stable activated sludge could be maintained using all the wastes from the Cherokee Plant. It was cautioned that the pH value of the raw wastes should be kept between 6 and 8. The investigators stated that a wide range of treatment performance could be obtained, and also predicted, for any given set of conditions as to suspended solids, retention times and BOD loadings. In disposing of excess biological sludges, filtration-incineration and anaerobic digestion were rejected as feasible operations (although sufficient reasons were not given) whereas aerobic digestion was thought to offer at least a partial solution to the sludge disposal undertaking (20).

Design criteria were necessary, and probability data were developed for Cherokee Plant wastewaters with respect to waste volume and BOD load and concentrations. The 90-percent high probability values of flows and loads were used to give treatment plant design criteria. The design volume of raw wastes was established as 3,200 m^3/day (0.84 mgd) and the BOD raw waste load as 6,100 kg (13,500 lb)/day. The 50 and 90 percent probability values of raw waste BOD strengths were 1,600 mg/l and 2,600 mg/l, respectively. Mixed liquor suspended solids in the aeration basins were assumed as 2,500 mg/l. The BOD discharge to the receiving stream was predicted to be 1,800 kg (4,000 lb)/day yielding a desired "at that time" BOD removal of 70.5 percent via activated sludge. At the "average" expected raw waste loading of 3,600 kg (8,000 lb)BOD/day, a BOD reduction of around 90 percent was predicted. It is noted that design retention in the aeration basin(s) was only 2.2 hr.

From these studies the investigators concluded that the activated sludge process appeared superior to other treatment methods for Cherokee. The process gave consistently "good" BOD reductions and recovered quickly when subject to toxic substances. Also, from the standpoint of ease and efficiency of operation, activated sludge was deemed the best approach for satisfactorily treating the fine chemical wastewaters from Danville (20).

The recommended activated sludge treatment facilities were constructed in the late 1950's. Various improvements have been made since then with significant modifications and add-ons to the system completed around December 1972, including a large roughing filter, secondary settling, and vacuum filtration and incineration facilities for handling and disposing of excess biological sludges. These changes resulted in improved waste treatment performance beginning in early 1973. Present waste treatment facilities are described below.

Current Waste Treatment--As of mid-1974, treatment of process wastes consisted of equalization, neutralization, biological treatment including a roughing trickling filter and activated sludge, and secondary settling. Sludge was disposed of by dewatering and incineration.

Process wastes flow into a wet well and are then pumped into a 136 m^3 (36,000 gal.) equalizing tank providing about 9 hr detention. Wastewaters in this holding basin are kept agitated by means of a 60 HP aeration support system. Three cooling towers with a total rating of 5,450 m^3/day (1,000 gpm) are also available adjacent to the equalizing tank for chilling the process wastewaters from 35 to 46°C (95 to 115°F) down into the range of 29 to 35°C (85 to 95°F), when found necessary, especially in the summertime. The Company reports the latter temperature range as being optimum for subsequent biological treatment. Process wastes entering the equalizing tank have a pH range of 2 to 12. Process flows are currently averaging 3,780 m^3/day (700 gpm or 1 mgd).

Equalized process flows enter a neutralization tank for dosing with sulfuric acid or caustic soda. This tank has a 85 m^3 (22,500 gal.) capacity and provides about 36 min detention.

Neutralized wastewaters are pumped to a roughing trickling filter tower 6.6 m (21.5 ft) high by 15.2 m (50 ft) in diameter. Impressed flow rate on the filter is 7,630 or 15,260 m^3/day (1,400 or 2,800 gpm), depending upon whether one or two pumps are used. The recirculation ratio around the filter is 1:1 or 3:1.

Trickling filter effluent flows into two aeration basins in parallel with a total capacity of 2,560 m^3 (675,000 gal) giving 16 hr waste detention at average flow. Aerators on both the activated sludge aeration basins and the equalizing tank include twelve 30 HP sparged turbine units and two 50 HP units for a total of 460 HP. Specifications on the system call for 100 percent recycle of sludge from the secondary clarification tank back to the activated sludge basins. The Company indicates that 5,000 to 6,000 mg/l MLSS are maintained in the aeration basins.

The activated sludge liquors receive final clarification in a single 15.2 m (50 ft) diameter tank having a capacity of 555 m^3 (146,500 gal.). Average detention time in this unit is 1.5 hr. Sludge underflow concentration is reported to be roughly 1 percent solids.

Excess biological sludges from the secondary clarifier are sent to a sludge thickener tank 16 m (50 ft) in diameter. Thickener supernatants are returned to the main treatment works. The sludge is concentrated to roughly 3 percent solids and then conditioned, dewatered and incinerated. Conditioning consists of the addition of $FeCl_3$ and lime. Conditioned sludge is passed through a pair of vacuum filters producing a sludge of about 16 percent solids content. Filtrates from the vacuum filters plus filter belt wash waters are returned back to main treatment. Dewatered and filtered biological sludge is mixed with mycelium at about 20 percent solids content recovered from within the fermentation operations and introduced into a 7-tier multiple hearth incinerator. Temperatures within the incinerator vary between 650 and 930°C (1200 and 1700°F) depending upon the particular hearth level. The Company in 1972 indicated that sludge loadings of around 41 kkg (45 ton)/day of activated sludge at 84 percent moisture content plus 46 kkg (51 ton)/day of mycelia sludge at 80 percent moisture content were being experienced. Design specifications for the incinerator are set at 80 kkg (88 ton)/day, which means that all sludges cannot be sufficiently handled by the incinerator and this unit is apparently underdesigned. Off-site disposal of sludges is likely necessary. The completely oxidized sludges coming out of the incinerator in the form of a fine ash are collected and scavenged to landfill. The above incineration system was not completed until February-March of 1973.

Water treatment plant sludges, various filter washings, scrubber effluent from the sludge incinerator with a flow rate of about 1,500 l/min (400 gpm), and ash slurry from the main boilers are discharged to a small lagoon located adjacent to the final discharge line of the plant. Overflow from the lagoon combines with spent cooling waters and treated process wastes before discharge to the Susquehanna River through Outfall 001. In April 1974 it was observed that this lagoon was almost completely clogged with solids, and little solids settling was occurring. Later the Company reported that a second settling pond was under construction. The State of Pennsylvania permit which represents the last authorization for waste discharge by the Cherokee Plant explicitely states that ... " settled solids shall at no time be permitted to accumulate in the sedimentation basin(s) to a depth greater than one-third that of the basin(s) as constructed, and the settled materials removed shall be handled and disposed of in a (satisfactory) manner ..."

Treated process wastes leaving the final clarifier, overflows from the small lagoon, and the relatively large volumes of spent cooling waters, all combine at about the same point just prior to discharge to the Susquehanna River via Outfall 001. Although analytical data exist for the combined discharge and for the treated process waste stream, virtually no separate sampling information could be secured from the Company on the small lagoon overflows and the spent cooling water stream. Significant waste loads are believed present in the latter two flows, however, this cannot be verified by available data. Waste concentrations in the process flows are about 15-20 times higher than reported for the combined effluents.

There is no disinfection or equivalent on the final waste discharge. Fecal coliforms are reported present but in low quantities. The Company indicates chlorination is not necessary because sanitary sewage in the last 2-3 years has been entirely diverted out of the Cherokee treatment works into the local municipal sewerage system.

WASTE LOADS

Current Production Levels

Company records indicate that the present waste treatment facility, including improvements completed in December 1972, has the following design criteria [Table F-1].

Table F-1.
Summary of Current Waste Treatment Plant Design Criteria[a]

Parameter	(kg/day)	(lb/day)
Influent Loads		
Flow	3,030[b]	0.8[c]
BOD	8,620	19,000
TSS	2,130	4,700
NH_3-N	1,130	2,500
Effluent Loads		
BOD	1,380	3,050
TSS	610	1,350
Removal Efficiencies		
BOD	84 percent	
TSS	71 percent	
Cooling Water Stream		
Intake Water BOD	590	1,300
Incremental BOD Added in Plant	450	1,000
Total BOD Load	1,040	2,300
Combined Effluent Loads		
Flow	75,700[b]	20.0[c]
BOD	2,430	5,350
TSS	610	1,350
NH_3-N	1,130	2,500
TDS	27,670	61,000

[a] All values are averages
[b] Flow in m^3/day
[c] Flow in mgd

Table F-2

Summary of Monthly BOD Data
Merck and Co., Cherokee Plant, Danville, Pa.
December 1972 - February 1974

Month	Process Wastes to Treatment				Raw Water Intake BOD		Combined Effluents				BOD Removal	
	Flow		BOD Load				Flow		BOD Load		Through Treatment [a/]	Overall [b/]
	(m^3/day)	(mgd)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(m^3/day)	(mgd)	(kg/day)	(lb/day)	(percent)	(percent)
						1972						
Dec.	3,260	0.86	5,585	12,312	146	321	68,500	18.1	1,930	4,255	67.9	65.9
						1973						
Jan.	3,520	0.93	7,051	15,545	202	445	71,500	18.9	2,802	6,177	63.1	61.3
Feb.	4,050	1.07	7,502	16,539	166	365	75,300	19.9	2,363	5,210	70.8	69.4
Mar.	4,010	1.06	6,658	14,678	216	475	83,300	22.0	1,991	4,390	73.3	71.0
Apr.	3,630	0.96	7,284	16,058	288	634	82,900	21.9	2,424	5,343	70.5	67.9
May	3,970	1.05	8,182	18,039	232	511	87,100	23.0	1,572	3,466	83.6	81.3
June	6,400	1.69	11,450	25,244	63	139	98,400	26.0	1,238	2,729	89.7	89.2
Average (First Half 73)	4,280	1.13	8,030	17,700	195	430	83,300	22.0	2,060	4,550	75.2	73.4
July	3,480	0.92	5,467	12,052	48	106	83,300	22.0	937	2,066	83.7	83.0
Aug.	2,910	0.77	6,242	13,760	223	492	93,100	24.6	1,119	2,466	85.7	82.7
Sept.	3,560	0.94	7,112	15,678	190	418	89,700	23.7	899	1,982	90.1	87.7
Oct.	3,520	0.93	6,691	14,750	124	273	87,800	23.2	1,545	3,406	78.8	77.3
Nov.	3,220	0.85	5,815	12,820	157	347	87,800	23.2	1,184	2,611	82.3	80.2
Dec.	3,260	0.86	6,424	14,163	148	326	85,900	22.7	1,251	2,759	82.8	81.0
Average (Second Half 73)	3,330	0.88	6,290	13,870	150	330	87,800	23.2	1,160	2,550	83.9	82.0
						1974						
Jan.	3,900	1.03	7,150	15,763	102	224	74,200	19.6	1,188	2,619	84.3	83.5
Feb.	4,320	1.14	7,667	16,903	131	288	75,700	20.0	1,568	3,457	81.3	79.9
Average, 74	4,130	1.09	7,410	16,330	120	260	75,000	19.8	1,380	3,040	82.8	81.7
Overall Average	3,780	1.00	7,080	15,600	160	360	82,900	21.9	1,600	3,530	79.7	77.9

a/ Effluent data for the treatment works was not available; therefore, actual BOD removals could not be computed. The percent BOD removal shown was based on a treated effluent load computed by subtracting the raw water intake load from the combined effluent load. This assumes no incremental BOD increase in the cooling water stream which is known to be incorrect. The computed values thus represent "minimum" removals and actual removals would be higher.

b/ Overall BOD removal efficiencies were based on a comparison of the combined effluent loads with the process waste loads to treatment plus the raw water intake loads.

Table F-3

Summary of Monthly TSS and Total Solids Data
Merck and Co., Cherokee Plant, Danville, Pa.
December 1972 - February 1974

Month	Total Suspended Solids (TSS)						Total Solids					
	Raw Water Intake		Combined Effluents		Net Increase		Raw Water Intake		Combined Effluents		Net Increase	
	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)
						1972						
Dec.	4,450	9,820	6,580	14,500	2,130	4,700	14,940	32,930	32,750	72,200	17,830	39,300
						1973						
Jan.	2,360	5,200	6,730	14,830	4,350	9,600	13,810	30,440	45,930	101,260	32,110	70,800
Feb.	2,490	5,480	3,390	7,470	900	1,990	16,800	37,030	33,370	73,570	16,560	36,500
Mar.	10,910	24,050	5,830	12,850	-5,080	-11,200	24,570	54,160	33,890	74,720	9,340	20,600
April	5,220	11,500	4,560	10,050	- 660	- 1,460	15,240	33,600	29,680	65,430	14,420	31,800
May	1,510	3,320	5,920	13,050	4,400	9,700	13,990	30,850	34,470	76,000	20,500	45,200
June	2,110	4,660	5,810	12,800	3,670	8,100	21,600	47,620	36,920	81,400	15,330	33,800
Average (First Half 73)	4,100	9,000	5,400	11,800	1,270	2,800	17,700	39,000	35,700	78,730	18,050	39,800
July	640	1,410	7,080	15,610	6,440	14,200	16,490	36,360	23,900	52,690	7,410	16,330
Aug.	1,020	2,240	1,310	2,880	270	600	29,640	65,340	44,940	99,070	15,290	33,700
Sept.	590	1,290	1,710	3,760	1,130	2,500	29,630	65,320	40,370	89,000	10,750	23,700
Oct.	620	1,360	1,580	3,480	950	2,100	29,650	65,370	44,170	97,380	14,380	31,700
Nov.	703	1,550	2,280	5,030	1,590	3,500	22,750	50,140	38,010	83,800	15,290	33,700
Dec.	3,840	8,470	7,390	16,300	3,540	7,800	14,670	32,350	36,000	79,370	21,320	47,000
Average (Second Half 73)	1,200	2,700	3,540	7,800	2,300	5,100	23,800	52,500	37,900	83,600	14,100	31,000
						1974						
Jan.	2,540	5,590	3,420	7,530	880	1,940	12,830	28,280	29,100	64,160	16,280	35,880
Feb.	1,740	3,830	1,820	4,010	80	180	13,620	30,020	25,800	56,870	12,180	26,850
Average, 74	2,100	4,700	2,600	5,770	500	1,100	13,200	29,200	27,400	60,500	14,200	31,400
Overall Average	2,700	6,000	4,400	9,600	1,600	3,600	19,400	42,700	35,300	77,800	15,900	35,100

Table F-4

Ammonia Nitrogen and Phosphorous Content[a/]
Merck and Co., Cherokee Plant, Danville, Pennsylvania
October 30 - November 15, 1973

Sample Point	Flow		NH_3 - N				Phosphorous		
	(m^3/day)	(mgd)	(mg/l)	(mg/l)[b/]	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)
Treatment Plant Influent	3,370	0.89	451	165-620	1,530	3,370	59	200	440
Treatment Plant Effluent	3,370	0.89	454	335-590	1,520	3,360	34	116	255
Combined Total Plant Discharges	90,500	23.9	23	16-31	2,070[c/]	4,570[c/]	2.2	195[c/]	430[c/]
Raw River Water Intake	90,500	23.9	0.30	0.10-0.65	24	53	0.2	21	46

[a/] All values shown are averages except for NH_3 - N range.

[b/] Range

[c/] Incremental increases over and above treatment plant effluents shown of 550 kg (1,210 lb)/day NH_3-N and 79 kg (175 lb)/day phosphorous. These incremental increases attributable to spent cooling water discharges, overflows from the small settling pond, or other miscellaneous unrecorded discharges.

Waste load data were available from the Company for the process waste stream before treatment, the raw water intake, and the combined plant effluent including spent cooling water. These data were evaluated for the December 1972 through February 1974 period of record. Monthly BOD data for this period are summarized in Table F-2. Total suspended solids and total solids data are summarized in Table F-3. Nitrogen and phosphorous data for the period October 30 through November 15, 1973 are summarized in Table F-4.

A review of the data in Table F-2 indicates that treatment performance improved by mid-1973 following completion of additional treatment facilities in December 1972 and full operation of the sludge incineration process. Monthly BOD treatment removal efficiencies ranged from 63 to 90 percent with an average of 80 percent. Because about 95 percent of the wastewater discharged by the Cherokee Plant is untreated or partially treated, the overall system BOD reduction is considered more important than the treatment plant reduction per se. The overall reduction averaged only 78 percent. In discussions with the Company during 1974, they indicated that conceivable theoretical BOD reductions as high as 99 percent could be attained, except that costs would be entirely prohibitive.

A comparison of observed waste loads [Table F-2] and plant design criteria [Table F-1] indicates that current process waste flows averaging 3,780 m^3/day (1.0 mgd) are about 25 percent higher than design hydraulic loading. The July 1973 monthly average flow of 6,400 m^3/day (1.69 mgd) was 111 percent over design.

With respect to BOD loads, the long-term average of 7,080 kg (15,600 lb)/day for raw process wastes is slightly below design. The design criteria [Table F-1] for the cooling water stream assumed a BOD load of 590 kg (1,300 lb)/day present in the raw water intake. This load has averaged only 160 kg (360 lb)/day. Adjusting the design criteria for this difference effectively reduces the design combined effluent BOD load to 2,000 kg (4,400 lb)/day. Average effluent BOD was 1,600 kg (3,500 lb)/day, somewhat below design levels.

The Company no longer analyzes for COD. However, based upon past experience, they estimate that the COD:BOD ratio for treatment plant influents should be about 2.0, and for final effluents it should be between 8 and 10.

Observed total suspended solids and total solids loads in the combined effluents [Table F-2] averaged substantially above design criteria [Table F-1]. The TSS loads were unexpectedly high.

The nitrogen and phosphorous data collected by the Company in October-November 1973, [Table F-4] demonstrate high levels of N and P both before and after treatment. Ammonia nitrogen concentrations are exceptionally high. Phosphorous removals for this period were about 40 percent through the treatment works whereas ammonia nitrogen removals were virtually zero. Ammonia-N loads leaving treatment averaged 1,540 kg (3,400 lb)/day, and 2,090 kg (4,600 lb)/day in the combined effluents. These levels are substantially above the Company design specifications [Table F-1]. Incremental increases of 550 kg (1,200 lb)/day ammonia-N and 80 kg (180 lb)/day phosphorous are contributed by the spent cooling water stream. It is curious to note that final ammonia-N discharges are appreciably greater than effluent BOD loads. In the past, ammonium salts had been used for waste neutralization purposes. According to the Company, this practice is no longer employed.

Future Production Levels

The large-scale expansion of the Cherokee Plant scheduled for completion during 1975-1976 will substantially alter production levels and associated waste loads. Waste treatment facility improvements will be needed to cope with the increased waste load. Merck and Co. has submitted waste treatment plans to the State of Pennsylvania. During 1973-1974, in various materials submitted to the State, the Company indicated a 35 percent expansion of plant facilities at Cherokee, but also requested the State for much more than a 35 percent increase in effluent waste load allocations for various parameters. The Company not only assumed that their existing treatment was adequate but also that their plans for future treatment were adequate. A number of important questions have been subsequently raised on this subject.

The Merck (1975) treatment plant design contemplates future full-scale process raw wastes of 4,540 m^3/day (1.2 mgd) containing 17,700 kg (39,000 lb)/day BOD; 12,300 kg (5,100 lb)/day TSS; 3,650 kg (8,050 lb)/day NH_3-N; 55,650 kg (122,700)/day TSS; and 4.5 kg (10 lb)/day of CN. The 4,540 m^3/day (1.2 mgd) flow figure already requires correction because the Company assumed a 1,500 m^3/day (0.4 mgd) increase due to 1-methyldopa production over and above an average 3,000 m^3/day (0.8 mgd) for existing production. However, the latter flow figure should be at least 3,780 m^3/day (1.0 mgd). The plans and specifications of the Company indicate their "to-be-expanded" waste treatment facilities would provide effluent loads of 2,500 kg (5,520 lb)/day BOD (a 85.8 percent reduction); 920 kg (2,025 lb)/day TSS (only a 50 percent reduction); 1,860 kg (4,100 lb)/day NH_3-N; 55,650 kg (122,700 lb)/day TDS (zero reduction); and 0.4 kg (1 lb)/day CN (a 90 percent reduction). The Company has in the past stated they will be achieving 90 percent or better removals of BOD, but the design plans themselves show only a 85.8 percent BOD removal to be expected. Comparing the above figures to design of the existing treatment plant, future raw waste load increases associated with the 1-methyldopa expansion are calculated as follows: Flow - 20 to 50 percent; BOD - 105 percent; TSS - 17 percent; NH_3-N - 75 to 220 percent; and TDS - a 115 percent increase. It is quite evident that more than 35 percent increases are involved, and the Company plans are not adequate to meet the effluent limitations that have been written into the Cherokee Plant NPDES permit as discussed below.

Based on an extensive data analysis, raw waste loads for current production levels and future levels for full l-methyldopa production have been determined as follows:

Parameter	1974-1975 Full Production (kg/day)	1974-1975 Full Production (lb/day)	1975-1977 Full Production (kg/day)	1975-1977 Full Production (lb/day)
BOD	8,600	19,000	17,700	39,000
COD	17,200	38,000	28,200	62,200
TSS	2,100	4,700	2,300	5,100
NH_3-N	-	-	3,650	8,050

DEVELOPMENT OF NPDES PERMIT LIMITATIONS

Because of the severity of the nitrogen problem at Cherokee, limitations on ammonia nitrogen have been necessarily established for the NPDES permit. With the l-methyldopa production expansion, the Company predicts a total equivalent raw ammonia-N waste load of around 3,670 kg (8,100 lb)/day). The permit has specified future ammonia-N discharges of 1,040 kg (2,300 lb)/day, representing ammonia-N reductions of 70 to 75 percent. Available technology strongly infers that ammonia nitrogen loads could be reduced even below these prescribed levels. Phosphorous discharges have not been constrained by the permit, although eventually this issue will receive increased attention.

In the NPDES permit, consideration has been given to limitations on metallic and trace ions for the combined Cherokee effluents in the future. Selected constituents are of real and potential concern predicted upon limited analyses made available by the Company on effluents and/or because of relatively high concentrations of these materials in the incoming plant water supply. Cyanides and phenolics can be of considerable importance in wastewaters associated with l-methyldopa production, and NPDES future limits have been set at around 0.15 mg/l. Iron and manganese levels are quite high in the raw water supply and because of relatively stringent State receiving stream criteria on these parameters, suggested limits have been given as 0.5 mg/l for both parameters. Iron contributions can also be significant in the wastewaters coming directly from the production of l-methyldopa. Sulfide limits have been utilized due to appreciable sulfate loads in the Cherokee effluents and this constituent has been set at a maximum of 0.5 mg/l. Additionally, maximum levels of chromium and aluminum were tentatively prescribed at 0.25 mg/l and 0.75 mg/l, respectively. These various limits are to be attained by 1967-1977. It is also noted from past data that sodium values are quite high in the Cherokee waste flows although no action has been taken on this parameter.

Temperature limits were considered but were not established because of the ability of the River to adequately absorb existing thermal loads. Fecal coliform limits of 1,000 organisms/100 ml were tentatively prescribed.

The future plans also predicted incremental increases in the spent cooling water waste streams of about 820 kg (1,800 lb)/day BOD and 320 kg (700 lb)/day NH_3-N. In view of the reported presence of only non-contact waters, these incremental loads were considered unacceptable for purposes of the NPDES permit. Accordingly, the Company promised corrective action. With these incremental loads, the Company had previously predicted future total effluent loadings of around 3,320 kg (7,320 lb) BOD/day and 2,180 kg (4,800 lb) NH_3-N/day. These loads have been substantially lowered in the NPDES permit.

Based upon the tentative future criteria currently being developed for the bulk pharmaceutical industry, together with other considerations, average daily load limits to be achieved by 1976-1977 for major parameters in the Merck, Cherokee Plant permit are as follows:

Parameter	Load (kg/day)	Load (lb/day)	Reduction (percent)
BOD			
Gross	1,200	2,700	94
Net	1,050	2,310	-
TSS (Net)	690	1,530	70
COD	5,440	12,000	81
Ammonia-N	1,040	2,300	72

PHARMACEUTICAL INDUSTRY

CASE HISTORY G

WYETH LABORATORIES
MARIETTA, PENNSYLVANIA
(BIOLOGICALS PRODUCTION AND DRUG FORMULATION PLANT)

WYETH LABORATORIES, MARIETTA, PENNSYLVANIA
(BIOLOGICALS PRODUCTION AND DRUG FORMULATION PLANT)

BACKGROUND AND PROCESSES

The Wyeth Laboratories pharmaceuticals manufacturing installation at Marietta, Pa., specializes in the production of vaccines and serums, but also formulates and packages a number of synthetic organics. A large majority of final product is packaged as parenteral (injectable) ampules. The facility, opened for manufacturing in May 1965, basically operates five days a week with a single-shift operation. Total employment is around 400 persons. The plant was visited by EPA, NFIC-Denver, in April 1974 to obtain information for use in drafting a NPDES discharge permit for the Company at the request of EPA, Region III.

Processes used to produce vaccines and serums consist of specialized culturing and growing of bacteria and viruses, converting these bacteria and virus into vaccines, immunization of animals, repeated testing, and packaging of the final products. Formulation of organic compounds (e.g. atropine sulfate) involves processes such as solubilization, filtration, testing, and packaging.

Types of vaccines most commonly manufactured at Marietta include flu, tetanus and smallpox vaccines. Cholera and other "exotic" vaccines are also produced by the facility on special request. Snake-bite serums used against a wide variety of North American snakes also constitute a fairly well-known manufacturing line. Synthetic organic compounds manufactured include atropine sulfate (an anticholinergic and mydriatic); the antihistamines; selected narcotics; heparin (an anticoagulant); phenobarbital, et. al. Marietta turns out extremely large numbers of ampules (1 to 2 ml. used as injectables) amounting to tens of millions annually.

During late winter and early spring, the plant manufacturers large batches of flu vaccine. This manufacturing is highly dependent upon purchase orders placed by local, State and Federal governments. About 25 persons are specifically engaged for 2 to 3 months in production of flu vaccine. During the remainder of the year these persons are diverted to other activities. Tens of thousands of eggs are used daily in producing flu vaccine.

Animal colonies at Marietta are reported to be steadily diminishing. This is attributed to certain vaccines now being successfully cultured and grown on beef broth rather than on animal forms as previously was necessary. Monkey colonies are no longer maintained at Marietta and the horse population is currently at a minimum level. Other animal colonies are maintained mostly for blood testing purposes.

WASTE TREATMENT AND CONTROL

Special waste handling procedures in the animal holding areas include the transfer of cow dung to incinerators; composting of horse manure with the compost eventually given away to nearby farmers; and the dry cleaning of small-animal cages with the droppings going to incinerators and the cages then being steamed and washed with an alkaline detergent-disinfectant. Floors and equipment in the animal holding areas are reported to be frequently washed and sprayed with various disinfectants including "OSWL," "Wescidine I" and "Terramine." Large animal carcasses are disposed of to an off-site rendering establishment. Discarded eggs and shells are collected into 190 l (50-gal.) drums and carted away to sanitary landfill. Liberal amounts of disinfectant are used in the egg collection operations. In the event of spills of concentrated vaccine solution or any other hazardous substance occurring within the animal housing areas or in the main pharmaceuticals plant, special isolation procedures can be quickly implemented. Isolation is followed by flooding affected floors and equipment with a strong hypochlorite solution for a minimum period of one hour. Routine plant procedures involve extensive autoclaving of glassware and associated refuse.

Wyeth indicates they have three main safety systems: 1) cleaning up spills immediately after occurrence; 2) air locks in individual preparation-packaging rooms together with a separate air conveyance and filtration system; and 3) activated sludge treatment of plant wastewaters followed by three hours of chlorination to give added guarantee in killing bacteria and virus. Some years ago, Wyeth conducted toxicological testing of the treated final effluents upon newborn mice to discern possible environmental effects. The Company reports all such tests were negative.

Process wastes, animal waste residues, boiler blowdowns and various spent cooling water streams averaging 227 m^3/day (60,000 gpd) are discharged to an activated sludge treatment facility. Final discharge is to Evan's Run, a tributary to the main branch of the Susquehanna River in Western Pennsylvania.

Spent process, domestic and cooling waters are combined, passed through a comminutor, and discharged to a 150 m^3 (39,500 gal.) equalization tank equipped with auxiliary aeration. The equalizing tank provides roughly an 18-hour detention time. Wastewaters are carried through the weekends and holidays, and consequently maximum level in the equalizing basin is generally reached late on Friday. Raw wastes are then passed into two parallel activated sludge aeration basins of 127 m^3 (33,600 gal.) capacity each although it has been observed that usually only a single basin is in operation at any one time. Wastewater detention in the activated sludge basins approximates 8 to 12 hours. Activated sludge effluents are settled within a circular clarifier with a capacity of 119 m^3 (31,400 gal.). The clarifier overflow rate is reported as 9.0 m^3/m^2 (220 gal./ft^2)/day based upon a (original) design hydraulic load of 490 m^3/day (130,000 gpd). Sludge is recycled from the secondary clarifier back to the aeration chambers. Excess biological sludge is sent to a small aerobic sludge digester. Stabilized sludge is taken to sanitary landfill. The final unit in the treatment plant consists of a chlorine contact basin of 64 m^3 (17,000 gal.) capacity giving 3.2 hours detention at design flow. However, there is considerable more detention at current wastewater flow rates. Residual chlorine is thought to be in the range of 0.75 to 1.0 mg/l.

During the visit of April 2, 1974, a murky and deep purplish-red color was observed in the chlorine contact chamber. The Company attributed this color to recent cleanout of solids in the equalizing basin. Contents of the chlorine contact chamber also appeared relatively stagnant. The degree of mixing in the chlorine contact tank could be improved. There was an abundance of chicken feathers in the secondary clarifier which were passing over into the chlorine contact unit together with other floating and suspended matter. The MLSS content in the aeration basin(s) have been reported in the range of 2,300 to 9,100 mg/l with values most often around 4,000 mg/l. The presence of liberal amounts of blood are suspect within the treatment plant. The treatment facility has a design BOD load of 127 kg (280 lb)/day equivalent to 150 kg (330 lb)/day ultimate BOD. It is noted that existing BOD loads are significantly below these figures.

WASTE LOADS

Performance of the wastewater treatment operations was evaluated for the January 1973 to February 1974 period of record. Monthly results for this period are summarized in the Table G-1. Even though raw waste loads entering the treatment system are relatively small, it was noted that both the hydraulic and organic waste loads varied widely from month to month. Flows ranged from a low of 127 m^3/day (33,600 gpd) in January 1973 up to 344 m^3/day (91,000 gpd) in July 1973, a ratio of 2.7 to 1. The mean wastewater flow was 205 m^3/day (54,100 gpd). Monthly BOD loads incoming to treatment were quite low averaging 7.5 kg (16.6 lb)/day, but ranging from 2.3 kg (5.0 lb) all the way up to 33.1 kg (73.0 lb)/day. The average COD raw waste load was 26.6 kg (58.7 lb)/day, and the monthly COD loads as for BOD varied widely, ranging from 11.3 kg (25 lb)/day in January 1973 up to 67.7 kg (149.2 lb)/day in July 1973, a ratio of 6 to 1. Biochemical oxygen demand concentrations both before and after treatment were amazingly low signifying the presence of either large amounts of cooling and washing waters in the system or, more probably, serious toxicity impact upon BOD test results.

Over the 14-month period of record, overall BOD, COD and TSS loadings leaving the treatment plant in the final effluents were 0.4, 13.2 and 5.9 kg (0.9, 29.0 and 13.0 lb)/day, respectively. Monthly BOD effluent loads varied from 0.1 to 1.0 kg (0.3 to 2.3 lb)/day whereas TSS effluent loads ranged from 2.3 to 9.8 kg (5.0 to 21.6 lb)/day. The COD/BOD ratios for the raw wastewaters were generally in the range of 4:1 to 8:1. This ratio for final effluents was in the range of 15:1 to as high as 100:1. These ratios were

Table G-1

Summary of Monthly Waste Treatment Performance Data
Wyeth Laboratories, Marietta, Pennsylvania
January 1973 through February 1974

	Raw Wastes							
	Flow		BOD			COD		
Month	(m^3/day)	(gpd)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)
Jan. 73	127	33,600	18*	2.3	5.0	90	11.3	25.0
Feb.	184	48,600	17*	3.1	6.9	68	12.4	27.4
Mar.	-	-	-	-	-	-	-	-
Apr.	142	37,400	65	9.2	20.3	90	12.7	27.9
May	202	53,400	24*	4.9	10.7	110	22.5	49.7
June	246	65,000	19*	4.6	10.2	100	24.5	54.1
July	345	91,100	96	33.1	73.0	196	67.5	149.2
Aug.	265	70,000	16*	4.2	9.3	109	28.8	63.5
Sept.	224	59,200	17*	3.9	8.5	148	33.2	73.1
Oct.	190	50,100	17*	3.2	7.0	158	30.0	66.2
Nov.	218	57,700	25*	5.5	12.1	126	27.6	60.9
Dec.	159	42,000	34*	5.4	12.0	132	21.1	46.6
Jan. 74	171	45,200	42	7.2	15.9	151	25.8	56.9
Feb.	189	49,900	60	11.4	25.1	151	28.6	63.0
Average	205	54,100	35*	7.5*	16.6*	126	26.6	58.7

	Treated Effluent									Waste Reduction	
	BOD			COD			TSS			BOD	COD
Month	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	(mg/l)	(kg/day)	(lb/day)	(percent)	(percent)
Jan. 73	3	0.4	0.8	49	6.2	13.6	48	6.1	13.4	84.0	45.5
Feb.	1	0.2	0.5	36	6.5	14.4	37	6.8	15.0	92.7	47.5
Mar.	-	-	-	-	-	-	-	-	-	-	-
Apr.	1	0.2	0.4	37	5.3	11.6	16	2.3	5.0	98.0	58.4
May	1	0.2	0.4	29	5.9	12.9	48	9.8	21.6	96.5	74.0
June	3	0.7	1.6	76	18.7	41.2	18	4.4	9.6	84.4	23.8
July	3	1.0	2.3	63	21.5	47.4	17	5.8	12.7	96.9	68.1
Aug.	2	0.5	1.2	60	15.9	35.1	21	5.5	12.1	87.2	44.7
Sept.	1	0.3	0.6	71	15.8	34.8	26	5.9	12.9	93.0	52.4
Oct.	2	0.3	0.7	51	9.8	21.6	21	4.0	8.9	90.0	67.4
Nov.	2	0.5	1.2	89	19.5	42.9	43	9.3	20.6	90.1	29.6
Dec.	1	0.2	0.4	64	10.1	22.3	21	3.3	7.2	96.5	52.2
Jan. 74	2	0.3	0.7	87	14.3	31.6	28	9.8	10.6	95.7	44.5
Feb.	1	0.1	0.3	116	21.9	48.2	48	9.0	19.8	95.2	23.5
Average	2*	0.4*	0.9*	64	13.2	29.0	30	5.9	13.0	92.3*	48.6

* Indicates toxicity effects on BOD tests.

extremely high. Importantly, during many months, the calculated BOD loads attributable to domestic sewage alone (from the plant employees) were higher than the measured total BOD raw loads entering the treatment plant. Artificially low BOD results were apparently being obtained both on the raw and final wastewaters due to toxicity. The overall BOD removal through the treatment plant from January 1973 through February 1974 was 92.3 percent, which, however, is considered rather meaningless in view of the toxicity issue. The overall COD removal of only 48.6 percent over this same period is considered far from desirable.

NPDES PERMIT CONDITIONS

Data on heavy metals supplied by Wyeth Laboratories on the Marietta wastewater effluents were less than sufficient to assess the impact of metals upon biological treatment efficiency and any other interferences related to potential toxicity. Some metals were in the marginally acceptable/objectionable range including aluminum, boron, chromium, iron, copper and mercury. Levels of metal ions were such that limits were not necessary on the NPDES discharge permit; however, more information is sought in the future.

Final effluent limitations to be reached by April 1976 as specified in the NPDES permit in terms of the average daily and maximum daily conditions are respectively: BOD - 3.2 and 5.0 kg (7 and 11 lb)/day; COD - 13.6 and 20.4 kg (30 and 45 lb)/day; and TSS - 5.9 and 9.1 kg (13 and 20 lb) /day. Fecal coliform limitations and bioassay testing have also been specified in the permit. With respect to nitrogen and phosphorous, these appear present in the final effluents as highly-oxidized forms; thus, no permit limits were specified.

PHARMACEUTICAL INDUSTRY

CASE HISTORY H

WYETH LABORATORIES
PAOLI, PENNSYLVANIA

(DRUG MIXING, FORMULATION AND PREPARATION PLANT)

WYETH LABORATORIES, PAOLI, PENNSYLVANIA
(DRUG MIXING, FORMULATION AND PREPARATION PLANT)

BACKGROUND

Around 1956, Wyeth Laboratories decided to relocate its drug formulation and packaging facilities from Philadelphia to Paoli, Pa., some 30 miles west. This move was completed in 1961. In contrast to the availability of a municipal sewerage system in Philadelphia, Company waste treatment facilities were required at the new location.

The Paoli facility is a typical pharmaceuticals formulation plant that prepares and formulates a wide range of medicinals, drugs and related compounds. Compounds comprise mainly synthetic organic materials together with some naturally derived substances. Final products are primarily oral medications in the form of tablets and capsules; however liquid solutions and suspension-in-liquids are also manufactured. A partial listing of final products manufactured, according to the best information available, is as follows.

- Various cough syrups
- Oral contraceptives
- Various penicillin formulations
- Analgesics
- Tranquilizers
- Aspirin
- Suppositories
- Eyewashes
- Flavoring agents
- Food colorings
- Magnesium stearate
- Meprobamate (tranquilizer)
- Oxazepam (tranquilizer)
- Cyclospasmol
- Phenacetin (antacid)
- Vitamin C
- Benzaldehyde
- Boric acid
- "Bismuth"
- Caffeine
- Codeine-containing products
- "Phenergan"
- Sodium benzoate
- Manitol
- Phenobarbital
- Pentritol
- Diethylstilbestrol

Major raw materials reported as being received into the Paoli plant include sugar, corn syrups, lactose, cocoa butter, gelatin (used in capsules), calcium, talc, kaolin, diatamaceous earth, thiourea, ethyl alcohol, glycerine, wine, sorbitol, aspirin, bulk penicillin, and various analgesics.

The plant essentially operates over a single shift, five days a week, and employs 1,450 persons. A skeleton staff is maintained during the second and third shifts and over weekends.

Treated effluent from the plant is discharged to a small creek tributary to Little Valley Creek in the Schuylkill River Basin.

Information presented herein was obtained from two engineering reports (29, 50) and a March 1974 plant visit by NFIC-Denver to gather information for development of a NPDES discharge permit.

WASTE TREATMENT AND CONTROL

Waste Sources

Waste characterization and treatability studies undertaken to provide the basis for the design of the new Paoli treatment facility identified the following probable sources of wastewaters (29, 50):

a) The formulation and bottling of liquid preparations.
b) The formulation of dry preparations being shaped into coated tablets, or made up into capsules, and subsequently packaged.
c) The formulation and packaging of various jelled preparations.
d) The product development laboratory.
e) The analytical laboratories.
f) Sanitary sewage, cafeteria residues and other domestic needs.

Spent organic materials were expected to consist chiefly of lactose, corn syrups, wine, sucrose, gelatin, cocoa butter, alcohol, together with contributions from the cafeteria, and sanitary wastes.

Cooling water is recycled through a large double unit cooling tower. System blowdown is discharged to the waste treatment system.

Initial Treatment System Design and Operation

Predicted wastewater flows and characteristics for the 1961 initial period of operation and for the 1966 design year as developed by the waste characterization study are summarized in Table H-1.

Table H-1

Projected Waste Loadings, Wyeth Labs (29)

Type Waste	Initial (1961)				Design (1966)			
	Volume		BOD		Volume		BOD	
	(m^3/day)	(gpd)	(kg/day)	(lb/day)	(m^3/day)	(gpd)	(kg/day)	(lb/day)
Process Wastes	121	32,200	38	83	193	51,000	63	138
Sanitary Wastes	74	19,500	17	38	114	30,000	27	60
Total	195	51,500	55	121	307	81,000	90	198

A summary of design criteria for the 1966 average conditions was given as:

COD strength - 450 mg/l
Flow rate - 371 l/min (98 gpm)
Sludge recycle rate - 136 l/min (36 gpm)
Aeration basin detention - 8.3 hr
Sludge stabilization time - 4.2 hr
Clarifier rise rate - 18.3 m^3/m^2/day (450 gal/ft^2/day)
Clarifier detention - 2.4 hr

Laboratory waste treatability evaluations showed that at certain F/M ratios the wastes exhibited toxic effects. To preclude toxicity to sludge micro-organisms, the preliminary studies indicated that an aeration time greater than 4 hr was necessary. An acclimated sludge was eventually developed to counteract toxicity. Water quality limits for the receiving stream necessitated that treatment should provide a minimum of 85 percent reduction of organic matter and removal of substantially all TSS, and toxic, odor and taste-producing materials. Since both process and sanitary wastes were generated from 8 AM to 5 PM on weekdays only, it was decided to segregate the process and sanitary flows, to accept the sanitary wastes on a demand basis, but to provide extensive equalization and holding of the process wastes.

Initial operation of the full-scale treatment facilities began in March 1961. This system provided separate conveyance of sanitary and cafeteria wastes into the treatment plant through a comminutor, with these wastes entering directly into the activated sludge aeration tanks. Process wastes were passed through a primary skimming basin, into one of two equalization tanks, and then pumped at a controlled rate to the aeration basins. Capacity of the equalizing tanks was three times the average daily process wasteflows. Four aeration basins were constructed, arranged in two parallel sets of two basins each. Overflows from the aeration basins passed to two final clarifiers operated in parallel. Settled effluents were chlorinated before final discharge. Biological sludges from the final clarifiers were bled to two aerated sludge stabilization tanks. Stabilized sludges were recycled to the activated sludge aeration basins.

In the initial months of treatment plant operation, operation of all aeration basins was found to be unnecessary; consequently, one of these tanks was converted to an aerobic sludge digester for handling excess biological solids. Sludges were ultimately removed from the treatment circuit via chemical conditioning, vacuum filtration and landfill disposal.

During 1961-1962, average monthly process waste flows ranged from 76 to 106 m^3/day (20,000 to 28,000 gpd). Sanitary flows approximated 95 to 132 m^3/day (25,000 to 35,000 gpd). From July 1961 through April 1962, monthly influent loads to the treatment facility ranged from 30 to 70 kg (67 to 154 lb)/day BOD and 46 to 98 kg (101 to 216 lb)/day COD. Treated effluent for this same 1961-62 period contained 1.5 to 2.7 kg (3.2 to 5.9 lb)/day BOD and 7.3 to 16.7 kg (16.0 to 36.8 lb)/day COD. Overall average waste removals were 96.1 percent for BOD and 83.7 percent for COD. Effluent TSS concentrations, in terms of monthly averages, ranged from 7 to 34 mg/l. The TSS level in the final effluent averaged 21.5 mg/l during this 1961-62 period.

The Company reported that somewhat lower BOD removals (i.e. 93 and 94 percent) were recorded when the strength of the wastewater entering the treatment facility was abnormally low. Under normal conditions, BOD removal was in the range of 97 percent and COD removal around 85 percent, which are impressively high (29). A later report gives treatment performance results covering the period January 1961 through February 1963 (50). This later record of 26 months shows an average hydraulic load of 190 m^3/day (50,000 gpd) with about 54 kg (120 lb) BOD/day entering treatment. The final effluent was said to be averaging about 12 mg/l BOD equivalent to 2.3 kg (5.0 lb) BOD/day and 95.8 percent BOD removal. Effluent COD was averaging around 80 mg/l.

Foaming problems attributed to the presence of detergents were experienced in the wastewater treatment plant. A number of foam-depressant chemicals were employed with only limited success including a waste silicone emulsion, sperm oil, isodecanol, and commercial antifoams. Next, surface sprays were installed at the head end of the final settlers to assist in breaking down the persistent foam layer, which solved the foaming at least on the clarifiers. A better solution was later devised, however, which involved converting one of the aeration basins into a foam collecting tank. Excess foam was collected from within the treatment circuit and broken down by mixing without aeration, and then fed to the aerobic digester. The foam was not as intense in the digester because of the higher solids levels. The digester was dewatered daily. Although detergents in the effluent were not reduced, nevertheless, operational difficulties were reported significantly lowered by these procedures (29, 50).

Current Waste Treatment

When inspected by NFIC-Denver in March 1974, several changes in waste treatment from the original design were noted. Sanitary wastes are now discharged to the equalizing basins along with process wastes. Air spargers have been added to the equalizing basins in the last year and a half to eliminate septic conditions during periods of low flow, particularly over weekends.

Process wastes enter a small collection chamber where flotable greases are skimmed off and collected. Sanitary wastes pass through a bar screen and communitor. Process and sanitary flows then combine before entering two equalization basins operated on a fill-and-draw basis. Combined flows are generally split, half into each equalizing basin. Each chamber is 280 m^3 (74,000 gal.) in size, providing a total of around 1.5 to 2.0 days detention. Although wastewater flows are generated only over about 10 hr each day and 5 to 5-1/2 days a week, the treatment system is operated continuously.

Equalized flows are fed into three activated sludge aeration basins, presumably operated in parallel, with each basin having a capacity of 47 m^3 (12,500 gal.). The three basins provide about 9 hr detention time when maintaining a 1:1 wastewater to sludge return ratio. A fourth 47 m^3 (12,500 gal.) tank serves as an aerobic sludge digestion chamber. The F/M ratio in the aeration basins is reported around 0.5. The MLVSS content is kept around 2,400 mg/l which is somewhat lower than expected. Secondary clarification capacity is 76 m^3 (20,000 gal.) equivalent to 4.5 to 5.0 hr detention. Recycle biological sludges from the secondary clarifiers are passed through an aerated sludge stabilization chamber of 38m^3 (10,000 gal.) size prior to return to the activated sludge aeration basins. A baffled chlorine contact tank provides about 30 min detention of final effluent, producing a residual chlorine of around 1 mg/l. Excess biological sludges accumulating within the treatment system are periodically removed by outside scavengers, presumably to public landfill. For the last month of available record (January 1974), process and sanitary flows averaged 243 and 93 m^3/day (64,100 and 24,700 gpd), respectively, for a total of 336 m^3/day (88,800 gpd), about 10 percent above design flow.

CURRENT WASTE LOADS

The Company has compiled sampling results from the Paoli treatment plant in the form of monthly reports made available to the regulatory agencies. The period of record from January 1973 through January 1974 was used in evaluating the treatment plant performance for NPDES permit preparation. These data are summarized in Table H-2.

A comparison of the 1973-74 data [Table H-2] with the waste loads given previously for 1961 shows that BOD loads and wastewater volume have roughly doubled in the past 12 years. Treatment plant capacity, believed based on predicted 1966 waste loads [Table H-1], was being exceeded by about 10 to 20 percent in 1973-74.

Biochemical oxygen demand and COD removals averaged 94.5 and 85.0 percent, respectively, during 1973-74 [Table H-2]. Raw waste TSS data were not collected; therefore, removal efficiencies could not be determined.

Table H-2

Summary of Average Monthly Wastewater Treatment Data
Wyeth Laboratories, Paoli, Pennsylvania
January 1973 - January 1974

Month	Flow		Influent Loads				Effluent Loads						Waste Removals	
			BOD		COD		BOD		COD		TSS		BOD	COD
	(m^3/day)	(gpd)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(percent)	(percent)
Jan. 1973	260	68,700	59	130	127	280	2	5	16	35	7	16	96.2	87.5
Feb.	327	86,400	106	234	252	556	4	9	24	52	17	38	96.1	90.6
Mar.	350	92,400	93	204	312	687	3	7	23	50	8	18	96.5	92.7
April	365	96,400	61	134	81	178	6	14	25	56	16	35	89.4	68.5
May	355	93,700	54	118	184	405	7	16	33	73	22	49	86.6	82.0
June	406	107,200	80	177	114	252	5	12	29	64	23	50	93.1	74.6
July	456	120,600	109	241	189	416	6	13	27	60	19	41	94.8	85.6
Aug.	475	125,500	176	387	222	489	10	21	33	72	28	62	94.5	85.3
Sept.	432	114,200	134	295	202	446	9	20	33	72	25	56	93.5	83.9
Oct.	363	96,000	120	265	174	383	4	8	15	34	9	19	97.0	91.1
Nov.	312	82,500	149	329	206	454	3	7	12	26	5	10	97.9	94.3
Dec.	315	83,200	103	227	196	433	3	7	28	62	23	50	97.1	85.7
Jan. 1974	285	75,400	115	253	184	406	7	16	53	117	34	76	93.7	71.2
Average of 13 months	316	95,500	104	230	188	414	5.4	11.9	27.0	59.5	18.1	40.0	94.5	85.0
Average of 1973 Months							5.3	11.6	24.8	54.7	16.8	37.0		

DEVELOPMENT OF NPDES PERMIT CONDITIONS

Based on a statistical evaluation of the 1973-74 data in Table H-2, permit conditions specifying average daily and maximum daily limits of 8.2 and 11.3 kg (18 and 25 lb)/day of BOD were recommended for the Paoli plant to be achieved by June 1, 1976. Corresponding limtis for COD were 36.3 and 54.4 kg (80 and 120 lb)/day, respectively. The COD:BOD ratio of raw wastewater has been averaging around 1.8 while this ratio for treated effluent has been in the range of 4.0 to 5.0. In EPA Effluent Guideline Limitations for other industries where conventional activated sludge, or particularly extended aeration, is employed for achieving Best Practicable Control Technology Currently Available, allowances have been given for somewhat greater TSS effluent loads as compared to BOD loads. Consequently, average daily and maximum daily limits for TSS were recommended for Paoli as 11.3 and 18.1 kg (25 and 40 lb)/day, respectively.

The presence of metallics and toxicity in the wastewaters may or may not represent continuing problems. The Company reports 2.5 mg/l lead in the final effluent together with 1.0 mg/l tin, 0.8 mg/l nickel, and 0.28 mg/l zinc, but these data are represented by a single analysis only. Lead has been limited in the NPDES permit to a maximum daily level by June 1976 of 0.2 mg/l. A number of metallics and other ions appear in the marginal range including nickel, zinc, tin, copper, iron, molybdenum, boron, mercury and possibly arsenic. Because of the unknown impact of metals and other pharmaceutical waste constituents, the recommendation has been made that fish survival tests be conducted twice annually, with further action to be taken if indicated necessary. Fecal coliform bacteria in the final effluent are consistently below 400/100 ml and should represent no problem.

PHARMACEUTICAL INDUSTRY

CASE HISTORY I

MCNEIL LABORATORIES, INC.
FORT WASHINGTON, PENNSYLVANIA

(DRUG MIXING, FORMULATION AND PREPARATION PLANT)

I-1-a

McNEIL LABORATORIES, INC., FORT WASHINGTON, PENNSYLVANIA
(DRUG MIXING, FORMULATION AND PREPARATION PLANT)

BACKGROUND AND PROCESS DESCRIPTION

McNeil Laboratories, Inc., a subsidiary of Johnson and Johnson, Inc., operates a drug formulating facility at Fort Washington engaged in the mixing, formulating, preparation and packaging of medicinals, drugs and associated products in dosage form for human consumption and use. Bulk raw materials (mostly synthesized organics) are received from domestic and foreign sources.

The plant has about 600 employees and is believed to be operated essentially five days a week. Two shifts are maintained by the manufacturing sectors while administrative and research functions employ only one shift. About 160 persons are engaged in research and laboratory quality control (roughly 20 percent of the total staff).

Seventy or more products are reported formulated by McNeil including liquid, semi-solid and solid forms. No biologicals are produced. All final products are intended for human use. An abbreviated listing of major types of products includes:

> various barbiturates, some "narcotic type" drugs, analgesics, Griseofulvin (an antibiotic), codeine (natural), various cough syrups and elixirs, intravenous and intramuscular sterile injection packages, anaesthesia solutions, diuretics, many different tablets and liquids, iron ox bile and carbolic acid (it is not known whether the latter two materials are raw and/or final products). The Company reported that over 1500 batches of various products may be formulated annually at this plant.

Significant colonies of animals (largely guinea pigs and mice) are maintained at this facility.

Apparently due to the startup of a new manufacturing plant in Puerto Rico or for other reasons, the Company has stabilized operations at the Fort Washington location. No plans for expansion are apparent in the forseeable future. A substantial production capacity increase occurred during the 1972-1973 period.

Water supply averaging 300 m^3/day (80,000 gpd) is obtained from a local water company. Of this total, 110 m^3/day (29,000 gpd) is used for processing, 114 m^3/day (30,000 gpd) for cooling, 38 m^3/day (10,000 gpd) for boiler feed supply and 38 m^3/day (10,000 gpd) for sanitary needs.

Major sources of wastewater include the washing of vessels and equipment and floor washdowns in the manufacturing area, cleanup of animal holding areas, and sanitary wastes including cafeteria wastewaters. Treated effluent flows to Sandy Run, a very small tributary of Wissahickon Creek in the Schuylkill River Basin of Pennsylvania. Sandy Run has been determined to have high fishing and recreational importance together with other recognized uses.

Background information, waste treatment data and effluent load data were compiled from two engineering consultant reports prepared in 1969 and 1972, an Industrial Waste Permit issued to the plant by the State on 22 October 1969, a permit application submitted to EPA in 1971, waste treatment plant operating data for the January 1973 through January 1974 period submitted by the Company, and other data obtained verbally from the Company during the plant visitation by NFIC-Denver in March 1974.

WASTE TREATMENT AND CONTROL

Waste Sources

Major wastewaters from the manufacturing area are reported to originate from the washing of vessels and equipment and floor washdowns. Much of the miscellaneous solids and liquids are discarded to landfill. Mechanical compactors are employed for certain forms of collectable solids. McNeil reports an overall chemical loss throughout all of handling and processing of only 1.0 to 1.5 percent.

In the animal area, cages are scrubbed dry and the collected materials including feces and animal carcasses are taken to an incinerator. Discarded animal bedding and straw are transported to landfill. The incinerator fumes are subjected to water scrubbing with effluent discharged to the central treatment works. The animal cages, housing assembly and rooms are given a final thorough cleaning and washing with the cages then sterilized or pasteurized. Extraneous hair is reported as a serious problem in the sewer collection system. The Company estimates that the animal holding operations can generate up to 76 m^3/day (20,000 gpd) of wastewater and 18 kg (40 lb) of BOD daily.

The cafeteria represents another potential area of waste contribution but these services mainly use "disposables" and kitchen facilities are minimal. Waste solids generated in the cafeteria area are usually bagged and hauled from the plant by a private garbage collector.

Main boilers operate on natural gas eliminating the need for bottom ash and fly ash disposal. The air supply at the plant is continuously filtered via bag filters for reuse in manufacturing areas.

The research activities use radionuclides. Spent radionuclides are secured and sent to the Atomic Energy Commission for final disposal.

Process and sanitary wastewaters are collected separately. Animal-handling area wastes are combined with the sanitary wastes prior to treatment. Cooling water is discharged to the process system.

Waste Treatment

A 15-year old activated sludge biological treatment facility treats all wastewaters from the McNeil installation. Major treatment units with their respective capacities and detention times are presented in Table I-1.

TABLE I-1. Treatment Units

Unit	No. of Units	Capacity (m^3)	Capacity (1,000 gal)	Detention Time
Primary Settling Tank	1	76	20	
Equalizing Basins	2	340	90	2.5 days
Aeration Tanks	2	199	52.5	<24 hours
Final Clarifiers	2	36	9.6	
Chlorine Contact Tank	1	24	6.3	2-4.5 hours
Sludge Thickener	1	50	13.2	
Aerobic Digester	1	81	21.5	

Process wastes are discharged to the primary settling tank. Flotables are skimmed and sent to the aerobic digester. Settled sludge is removed to the sludge thickener that also serves as a storage tank. The settled process wastes flow to the equalizing basins which are operated on a batch basis with the inflow being received into one tank while the contents of the other tank are discharged to the secondary treatment portion of the plant. The equalizing tanks enable necessary carryover of flow in the treatment system during night hours but especially over the non-processing weekends. The equalizing chambers are equipped with air diffusers to preclude septic conditions during waste holding.

The combined sanitary sewage and animal handling wastes pass through a comminutor for shredding of solids and are then combined with the effluent from the equalizing tanks and discharged to the aeration tanks. One or both aeration tanks can be employed but past operations have involved use of a single tank providing 24 hours waste detention or less, predicted upon the rate of flow. The aeration basins are equipped with sludge recycling and provisions for nutrient feed, if found necessary. The mixed liquors leaving aeration receive final settling in a pair of clarifiers arranged in parallel. Sludge is either returned to the aeration basins or the excess is wasted to the aerobic digester. The clarified effluents pass through a chlorine contact tank before final discharge. Chlorine tank detention times under design conditions are in the range of about 2 to 4.5 hours. Design plans call for 1 mg/l chlorine residual in the final effluent.

Primary sludge essentially receives thickening only. Secondary sludge is sent to the aerobic digester with excess sludge transferred to the sludge thickener. Supernatant from the thickener is displaced to the primary clarifier. Sludge is unloaded from the overall system by means of scavenger takeoff from the bottom of the sludge thickener tank with ultimate disposal by landfill.

Process waste inflow and final treatment plant effluent are measured. During 1967-68, average total plant influent was only 134 m^3/day (35,500 gpd) consisting of 117 m^3/day (31,000 gpd) of process wastes and 17 m^3/day (4,500 gpd) of sanitary and animal-handling wastewater. Average plant inflow in 1973 was 265 m^3/day (70,000 gpd). During the prime eight hours of the working day, the inflow rate was usually 2.5 to 3 times the average daily inflow.

As best as can be determined, the criteria used for the design of the treatment facility were: flow 348 m^3/day (92,000 gpd); influent BOD, 82 kg (180 lb)/day; BOD reduction, 95 percent; effluent BOD, 15 mg/l; effluent TSS, 30 mg/l.

WASTE LOADS

Table I-2 summarizes average final effluent data contained in a permit application submitted to EPA in 1971. Effluent loads for the McNeil formulation plant are very low in comparison to typical bulk pharmaceutical manufacturing installations.

Table I-2. Permit Application Data, 1971

Parameter	Concentration (mg/l)	Load	
		(kg/day)	(lb/day)
Flow	(257 m^3/day or 68,000 gpd)		
BOD	14	4	8
COD	66	17	38
TSS	26	7	15
TDS	510	132	290
NO_3-N	14	4	8
Total P	19	5	11
Sodium	72	19	41

The June 1972 engineering evaluation of Company sampling data for the period September 1971 through 1972 indicated that the waste treatment facility was achieving an average BOD removal of 93.5 percent and was achieving a 95 percent reduction about two-thirds to 80 percent of the time. The mixed liquor suspended solids concentrations in the aeration basin were in the range of 1,100 to 4,000 mg/l. Final effluent BOD averaged about 9 mg/l. The maximum average rate of flow acceptable into the McNeil treatment plant was judged to be around 340 to 378 m^3/day (90,000 to 100,000 gpd). During March 1972, the average total soluble phosphorous leaving the plant was found to be about 27 mg/l (as PO_4) compared to the State suggested limit of 0.5 to 1.0 mg/l. The phosphorous limitations were recognized as representing a serious constraint and challenge to the Company. In-plant controls on phosphorous sources and advanced physical-chemical treatment were given brief consideration by the Company.

The most extensive series of waste treatment performance data available was from the Company's monthly report sheets on the waste treatment plant. The data indicated that there was ample reserve in treatment capacity up through the last plant production expansion. However, beginning in 1973, treatment system overloads occurred. The period of record most appropriate for preparation of the McNeil NPDES permit was considered to extend from January 1973 through January 1974. Results of a detailed analysis made on this data [Table I-3] show that the activated sludge treatment works at McNeil Labs were doing surprisingly well in spite of incoming waste loads in excess of BOD and hydraulic design conditions on a number of occasions in 1973. Overload conditions were probably most severe during March and August, 1973 but also occurred on a number od days in May, November and other months (individual daily values not given herein). Flow quantities exceeded 379 m^3/day (100,000 gpd) a significant number of times. Design capacity of the activated sludge plant was assumed to be 348 m^3/day (68,800 gpd); the remainder was process waste. The COD/BOD ratio in the incoming feed to the treatment plant varied from 2.0 to 3.7 averaging 2.5. The ratio of COD/BOD in the final effluents varied from 2.2 to 10.9 averaging 4.3. The overall average COD removal was higher than expected at 87.7 percent. Without overload, the McNeil system could have likely provided an average BOD reduction of 93-94 percent and a 89-90 percent COD reduction. The calculated concentrations of BOD, COD and TSS based upon average loadings of 3.3, 12.2 and 3.5 kg (7.2, 26.9 and 7.7 lb)/day, yield respective values of 12.5 mg/l, 47 mg/l and 13 mg/l. These concentrations would appear quite acceptable.

DEVELOPMENT OF NPDES PERMIT LIMITATIONS

State Effluent Limitations

State requirements and recommendations for final effluents from the McNeil, Fort Washington installation applicable in 1973-1974 were described as follows: BOD - minimum of 95 percent removal and concentrations not to exceed an average of 15 mg/l and a maximum of 30 mg/l at any time; total soluble phosphorous (as PO_4) - the average not to exceed 0.5 mg/l with an allowable maximum of 1.0 mg/l; and iron - a maximum allowable of 7.0 mg/l. Recent information indicates the phosphorous limits no longer apply to the McNeil situation. These phosphorous limitations would be extremely difficult and costly to attain, especially for a plant of this size.

Table I-3

Monthly Waste Treatment Conditions

McNeil Laboratories, Inc., Fort Washington, Pennsylvania

January 1973 - January 1974

Month	Flow		Influent Loads				Effluent Loads						Waste Removals	
			BOD		COD		BOD		COD		TSS		BOD	COD
	(m^3/day)	(gpd)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(kg/day)	(lb/day)	(percent)	(percent)
Jan. 1973	249	65,900	74	164	155	342	5.1	11.2	17.7	39.0	2.6	5.8	93.0	88.7
Feb.	271	71,700	41	90	103	226	6.8	14.9	23.0	50.6	4.7	10.4	83.2	77.3
Mar.	289	76,300	67	147	197	433	10.0	22.1[a]	47.5	104.8[a]	10.7	23.6[a]	85.0	75.8
April	265	70,100	41	91	117	257	5.2	11.5	24.7	54.4	3.5	7.7	87.5	75.9
May	251	66,300	124	273	265	584	2.3	5.1	7.4	16.3	1.3	2.9	98.3	98.1
June	268	70,800	52	115	106	234	3.7	8.1	9.6	21.2	2.1	4.7	93.1	91.2
July	289	76,400	56	123	111	245	2.4	5.4	5.4	12.0	4.5	9.9	95.7	95.3
Aug.	295	78,000	22	48	80	177	1.6	3.6	10.2	22.4	3.7	8.1	92.4	87.5
Sept.	278	73,400	50	111	116	255	2.2	4.8	9.7	21.3	5.8	12.8	95.8	91.8
Oct.	279	73,800	30	66	69	152	4.4	9.8	11.3	25.0	5.1	11.3	85.2	84.2
Nov.	286	75,500	95	210	210	462	2.4	5.2	6.4	14.2	4.6	10.1	97.4	96.8
Dec.	210	55,500	70	154	185	408	2.0	4.4	44.8	98.7[b]	2.9	6.4	96.9	-
Jan. 1974	184	48,600	29	57	84	186	.8	1.8	8.9	19.7	1.0	2.3	96.8	89.6
Average	260	68,800	-	-	-	-	3.3	7.2	12.2	26.9	3.5	7.7	92.4	87.7
90 Percent High Value	315	83,300	-	-	-	-	6.1	13.6	23.0	50.7	6.0	13.2	-	-

a/ March values discounted because of critical hydraulic and organic overload on treatment works during a significant portion of the month.

b/ Analytical results questionable.